

[illegible]

Figure 1B

T	O	T	V	G	O	M	L	N	O	E	P	C	V	L	P	F	T	M	G	R	T	F	V	S	C	T	T	E	G	R	O	D	G	M	L	M	C	S	
970	980	990	1000	1010	1020	1030	1040	1050	1060	1070	1080	1090	1100	1110	1120	1130	1140	1150	1160	1170	1180	1190	1200	1210	1220	1230	1240	1250	1260	1270	1280	1290	1300	1310	1320	1330			
A	A	C	C	A	G	T	T	A	C	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T			
1340	1350	1360	1370	1380	1390	1400	1410	1420	1430	1440	1450	1460	1470	1480	1490	1500	1510	1520	1530	1540	1550	1560	1570	1580	1590	1600	1610	1620	1630	1640	1650	1660	1670	1680	1690				
T	F	S	M	V	E	O	D	O	K	V	S	F	C	T	D	M	T	V	L	V	O	T	O	G	G	M	S	M	G	A	L	C	M	F	P	F	L	T	M
1700	1710	1720	1730	1740	1750	1760	1770	1780	1790	1800	1810	1820	1830	1840	1850	1860	1870	1880	1890	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000	2010	2020	2030	2040	2050				
C	A	C	A	G	T	T	A	C	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T		
2060	2070	2080	2090	2100	2110	2120	2130	2140	2150	2160	2170	2180	2190	2200	2210	2220	2230	2240	2250	2260	2270	2280	2290	2300	2310	2320	2330	2340	2350	2360	2370	2380	2390	2400	2410	2420	2430		
M	M	M	V	T	O	C	T	S	E	G	R	R	O	M	M	K	M	C	G	T	T	O	M	V	O	A	D	O	K	F	G	F	C	P	M	A	A	M	E
2440	2450	2460	2470	2480	2490	2500	2510	2520	2530	2540	2550	2560	2570	2580	2590	2600	2610	2620	2630	2640	2650	2660	2670	2680	2690	2700	2710	2720	2730	2740	2750	2760	2770	2780	2790	2800	2810		
C	A	C	A	G	T	T	A	C	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T		
2820	2830	2840	2850	2860	2870	2880	2890	2900	2910	2920	2930	2940	2950	2960	2970	2980	2990	3000	3010	3020	3030	3040	3050	3060	3070	3080	3090	3100	3110	3120	3130	3140	3150	3160	3170	3180	3190		
E	I	C	T	F	M	E	G	V	M	Y	R	I	G	O	Q	W	O	K	O	M	D	M	G	M	M	R	C	T	C	V	G	M	G	R	G	E	M	T	
3200	3210	3220	3230	3240	3250	3260	3270	3280	3290	3300	3310	3320	3330	3340	3350	3360	3370	3380	3390	3400	3410	3420	3430	3440	3450	3460	3470	3480	3490	3500	3510	3520	3530	3540	3550	3560	3570		
G	A	A	T	S	O	L	R	O	O	C	I	V	O	O	I	V	M	V	N	D	T	F	M	K	M	E	E	G	M	M	L	N	C	T	C	F	G	I	
3600	3610	3620	3630	3640	3650	3660	367																																

[illegible]

Figure 1D

[illegible]

[illegible]

[illegible]

Figure 1H

36
G K T Y N V G E Q W Q R E Y L O A I C S C T C F G G Q R G V R C D M C R P C G
TQBBAGACATACCAOSTAGBAGACASTBGCAGABABAAATATC TQBBTQCCATTTC TQCTQCCATTCCTT TQBAQCCCAQDQDQDQCT TQCAACTTQDQCCAGACCTTQDQDQ
6730 6740 6750 6760 6770 6780 6790 6800 6810 6820 6830 6840
E P S P E G T F G Q S Y N Q Y S Q R Y N Q R Y N F N V M C P I E C F M P L D V O
TGAQDQAGTQDQBAQDQAC TACTQDQDQAGTQCTACACQDQAGTATCTCABAGATQDQCATCAGAGAGAACAC TAAATGT TAAI TQDQCAATTCAGTTCCT TCACTTTAGATG TCA
6850 6860 6870 6880 6890 6900 6910 6920 6930 6940 6950 6960
A D R E O S R E
GQCTCAGACAGACAGATTQDQDQAGAGTAAATCATCTTTQDCAATQDQAGAGAACABCATCTCTCTCTQDQCAAGATQCATCT TAACTQDQAGTATGT TACQCAQDQCCAGCTTACAGTCTCTCT
6970 6980 6990 7000 7010 7020 7030 7040 7050 7060 7070 7080
TTCTTTCTTAQDQDCTTTCTCTQDQAGAGAGTCTCTQDQAGCTTCAGCTCAACTCAGCTCTQDQCAQDQCATCTQDQAGAGTTCCTCTQDQAGGTTTCTCTCA TAAATCAGQDQCTQDQCACT
7090 7100 7110 7120 7130 7140 7150 7160 7170 7180 7190 7200
QCCIGTTCTGCTTQDQAGTATTCATAAADQDQCTCAGTATTTTAAATCAGAGTATCTTAAATCAGATTTQDGTTCQDQCATCAATQDQCAQDQCATATQDQCAQDQCAAGATQDQCAATGTTTTCATAT
7210 7220 7230 7240 7250 7260 7270 7280 7290 7300 7310 7320
GATATGACCAAAATTTTAACTAGQDQAGAGTCAQDQCAACACTCTCTCTTTTCACTTAAGTCTCTQDQDQDQDQCAATACCTGAGACACAGCATGCTTGT TACTGTCTATATTTTAAATATATDCA
7330 7340 7350 7360 7370 7380 7390 7400 7410 7420 7430 7440
CAGTACTCACTTTTCTCAATGATGCTAGTAAATQDQCTAGAAATATCTTCTCTTACTGTTATTTATCATATTTTCTCCAGATTTTCTTACQDQCAAAAB TGTATTCAAAACACTTACT
7450 7460 7470 7480 7490 7500 7510 7520 7530 7540 7550 7560
ATQDQGTGTAGAGQEAATTTQGTATATATATCTGTQDQGTGATTAATTTTATACCTGATCTGTCQDQCAQDQCTTACTACTGTQDQCAAGACACTGTTT TAA TAAAGATTTTACAT TQDQCA
7570 7580 7590 7600 7610 7620 7630 7640 7650 7660 7670 7680
AAAAAAAAAAAAAAAAAAAA
1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800

Figure 2A

Pair 1
 0 1 5'- AATTCATATGCGGCAAGCAATGGTTACGCCCAAGTCCCGGTGGCTGTCAAGCAAGCCCGTT - 3'
 0 2 3'- GTATACGTCGCGTGGTTTACCAAGTCGGGGTCAGGGGCCACGACAGTCAGTTTCGTTGGGGCCAACAATA - 5'

Pair 2
 0 3 5'- GTTATGACAAATGGAAACACTATCAGATAAATCAACAGTGGGAGGGACCTACCTAGGTAATGTGTG - 3'
 0 4 3'- CTGTTACCTTTTGTGATAGTCTATTTAGTTGTACCCCTCGGCTGGATGGATCCATT - 5'

Pair 3
 0 5 5'- GTTTGTACTTGTATGGAGGAGCCGAGGTTTAACTGGGAAGTAAACCTGAAGCT - 3'
 0 6 ACACAACCAACATGACAAATACCTCCTTCGGTCCAAATTGACGCTTTCATTGGGACTTCGACTTCTCT - 5'

Pair 4
 0 7 5'- GAAGAGACTTGTGACAAAGTACACTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCTCTAA - 3'
 0 8 3'- GAACGAACCTGTTCAATGACCTTGTGATGGCTACCCCACTGTGATACTCCAG - 5'

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Figure 2B

Pair 5

09 5'- GACTCCATGATCTGGGACTGTACCTGCCATCGGGGCTGGGCGAGGGAGATAGCTGTACC - 3'
010 GATTCTGAGGTACTAGACCCCTGACATGGACGTAGCCCCGACCCCGCTCCCTTATTC - 5'

Pair 6

011 5'- ATGCCCAACGCTGCCATGANGGGGTGAGTCTCCTACCAGATTGGTGACACCTGGAGGAGACCACATGAGACT - 3'
012 GACATGGTAGCGTTTCGGACGGTACTTCCCCCAGTCAGGATGGTCTAACCCACTGTGGACCTCCTCTGGTGATCTCTGALCACCAG - 5'

Pair 7

013 5'- GGTGGTTACATGTTAGAGTGTGTGTCTTGGTATGGAAAGGAGATGGACCTGCAAGCCCATAGCTGAG - 3'
014 3'- TGTACATCTCACACACACAGAACCATTAACCTTTCCCTTACCTGGACGTTTCGGGTATCGGACTCCTAG - 5'

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Figure 3

Synthesis of F.N. Gene (14 - 472 b.p.)

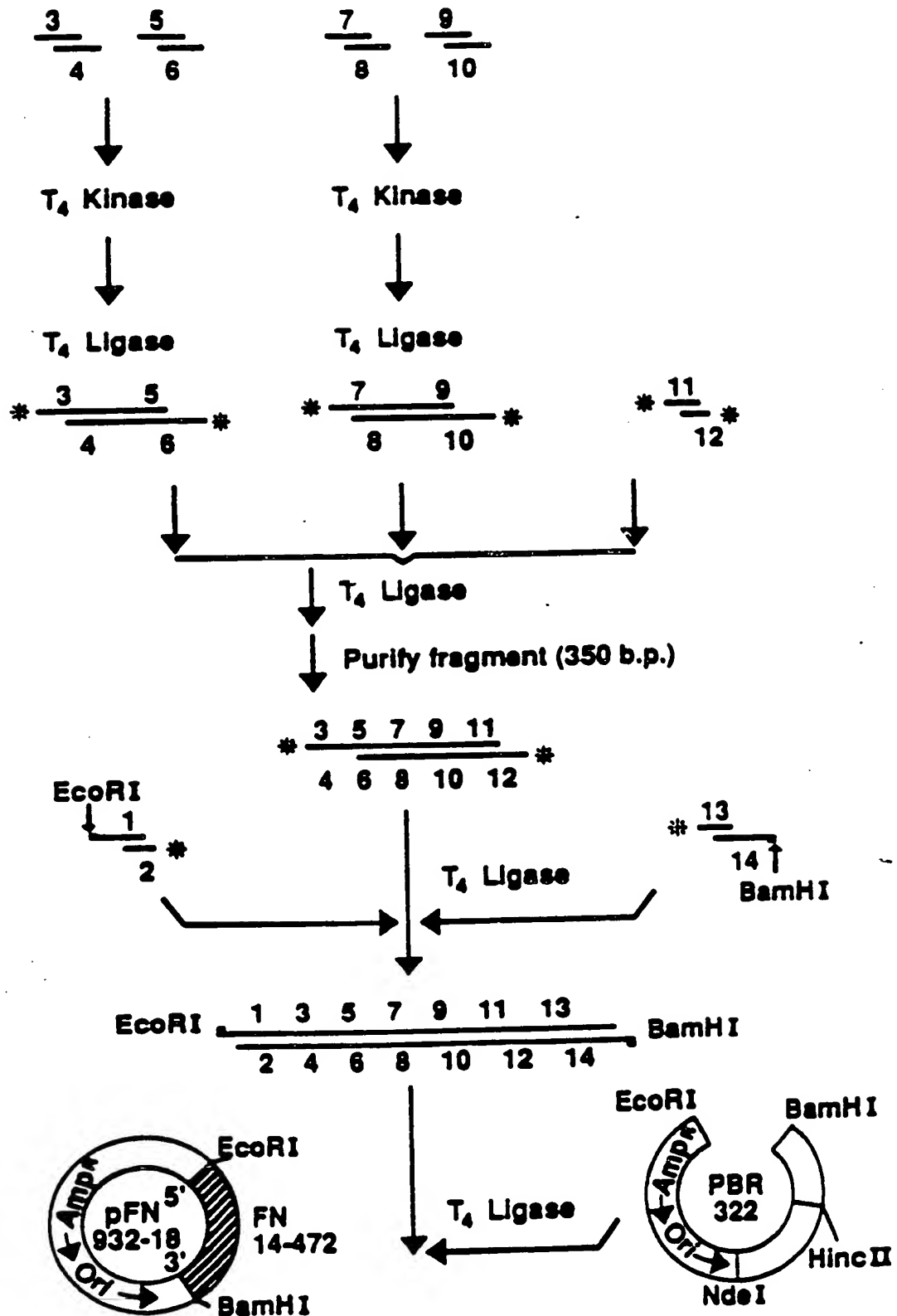
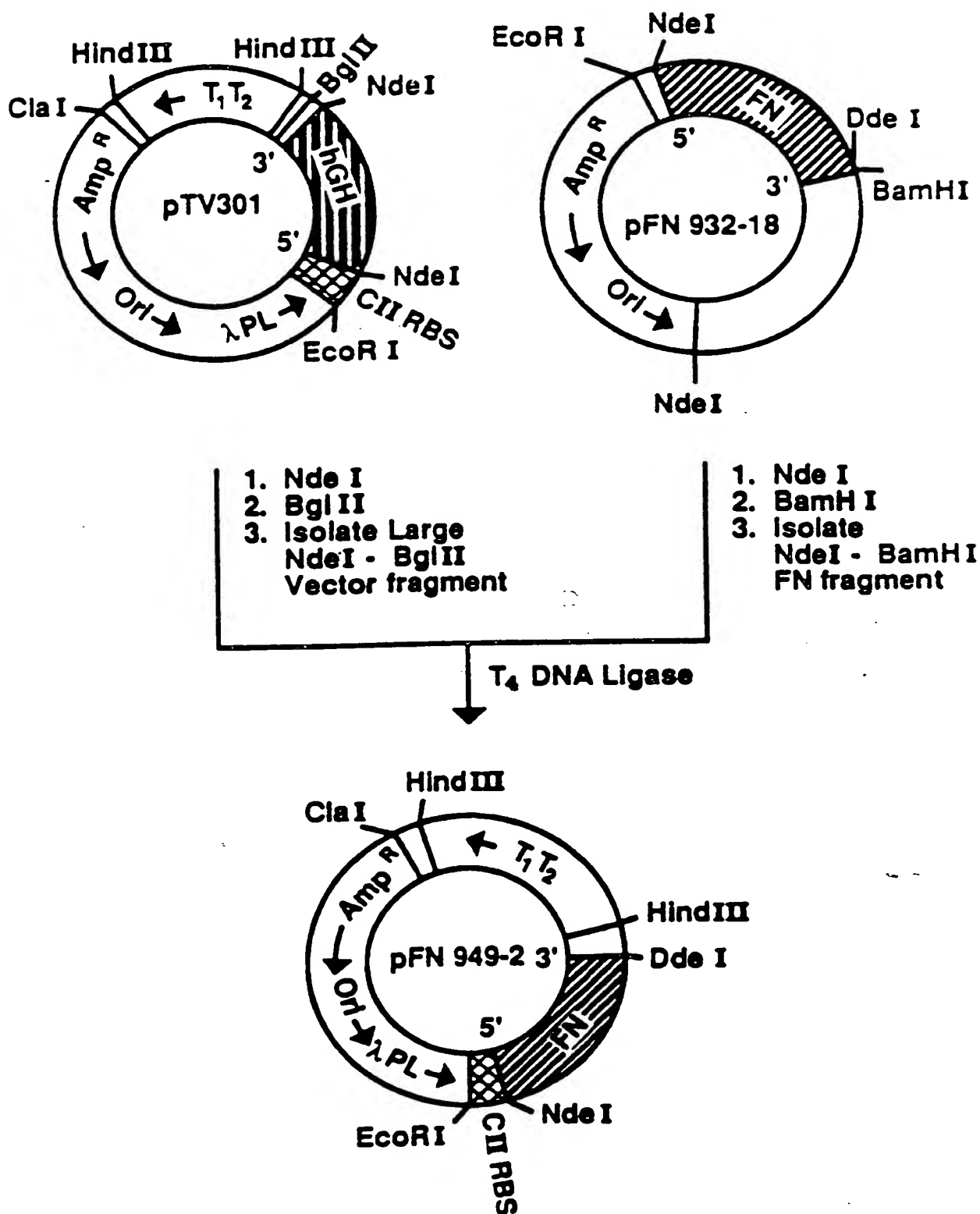
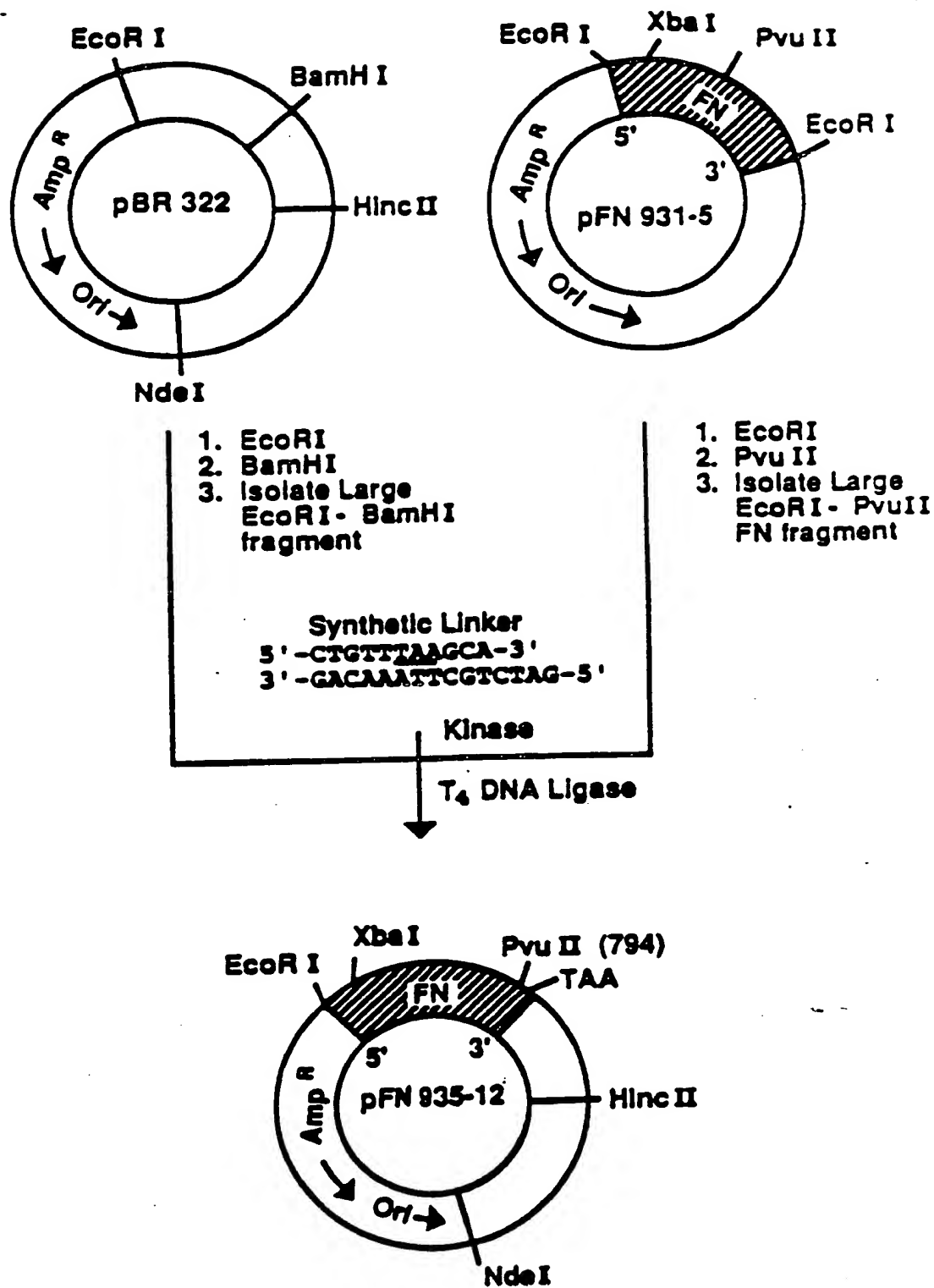


Figure 4



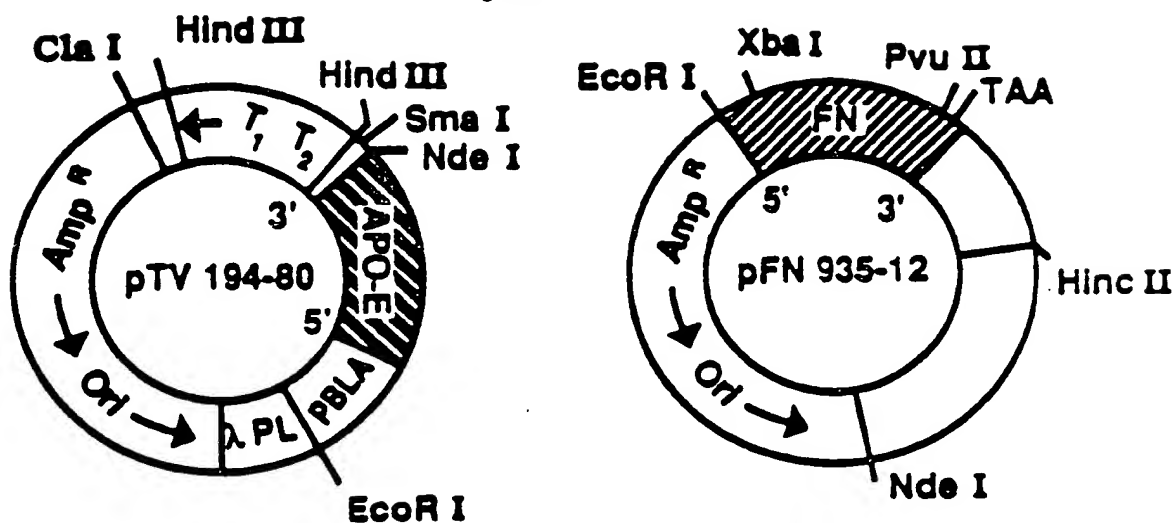
0049291-012700

Figure 5



0049291.01200

Figure 6



1. EcoR I
2. Sma I
3. Isolate large
EcoR I - Sma I fragment

1. EcoR I
2. Hinc II
3. Isolate
EcoR I - Hinc II
FN fragment

T₄ DNA Ligase

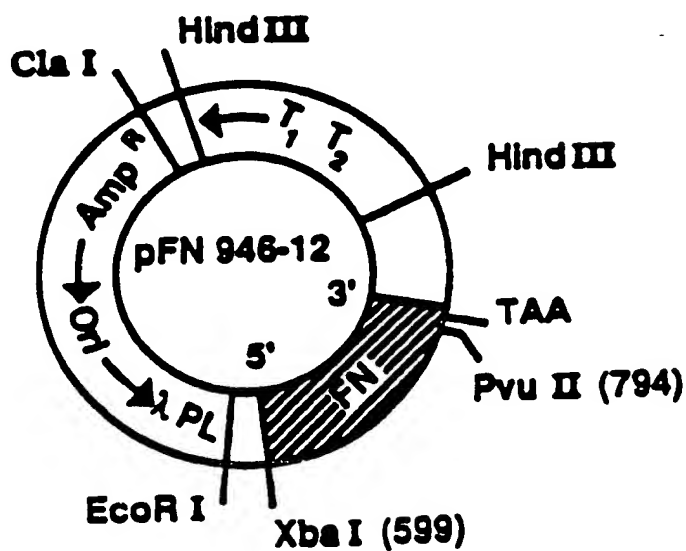
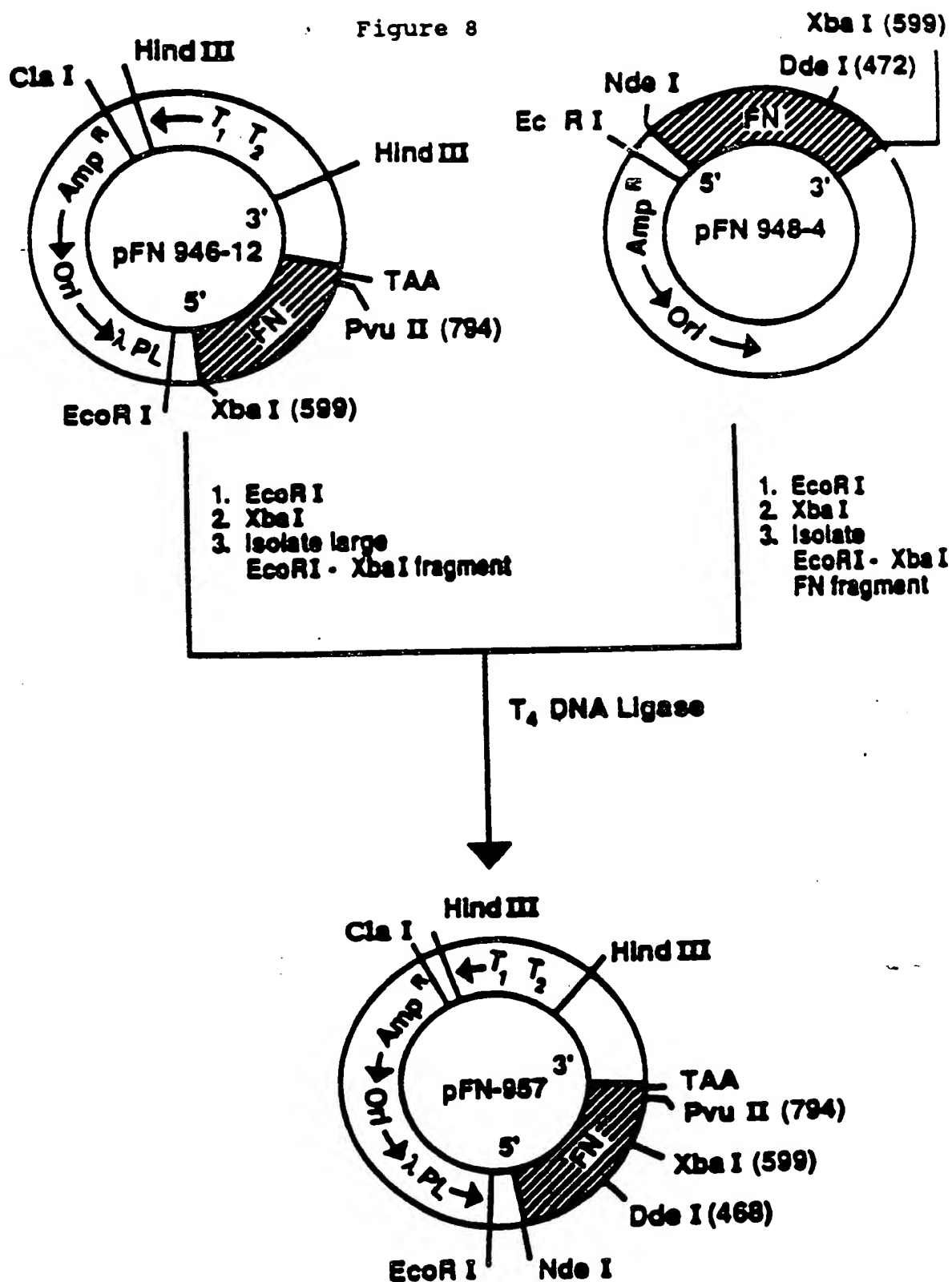


Figure 8



004997-012700

Figur 9

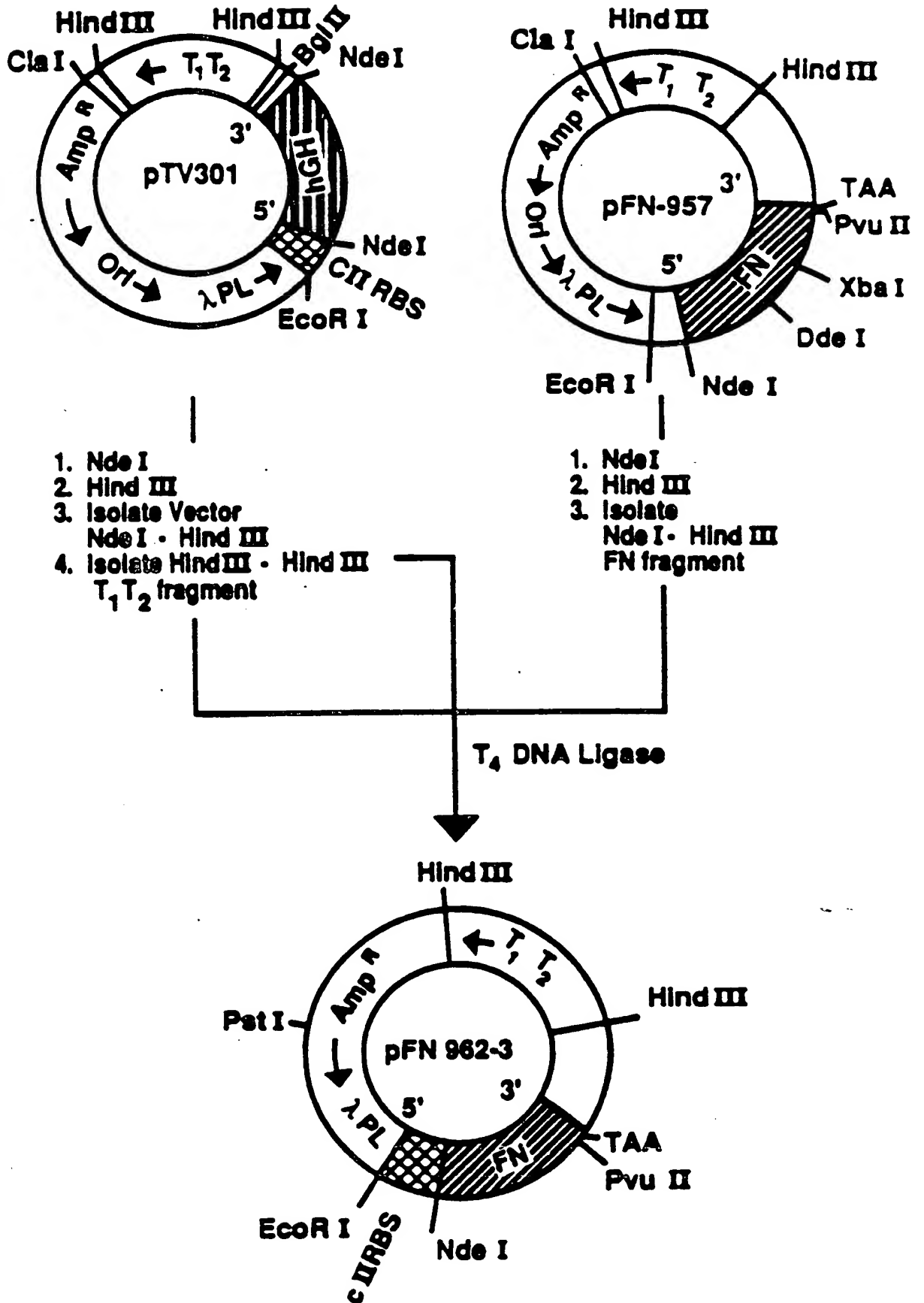
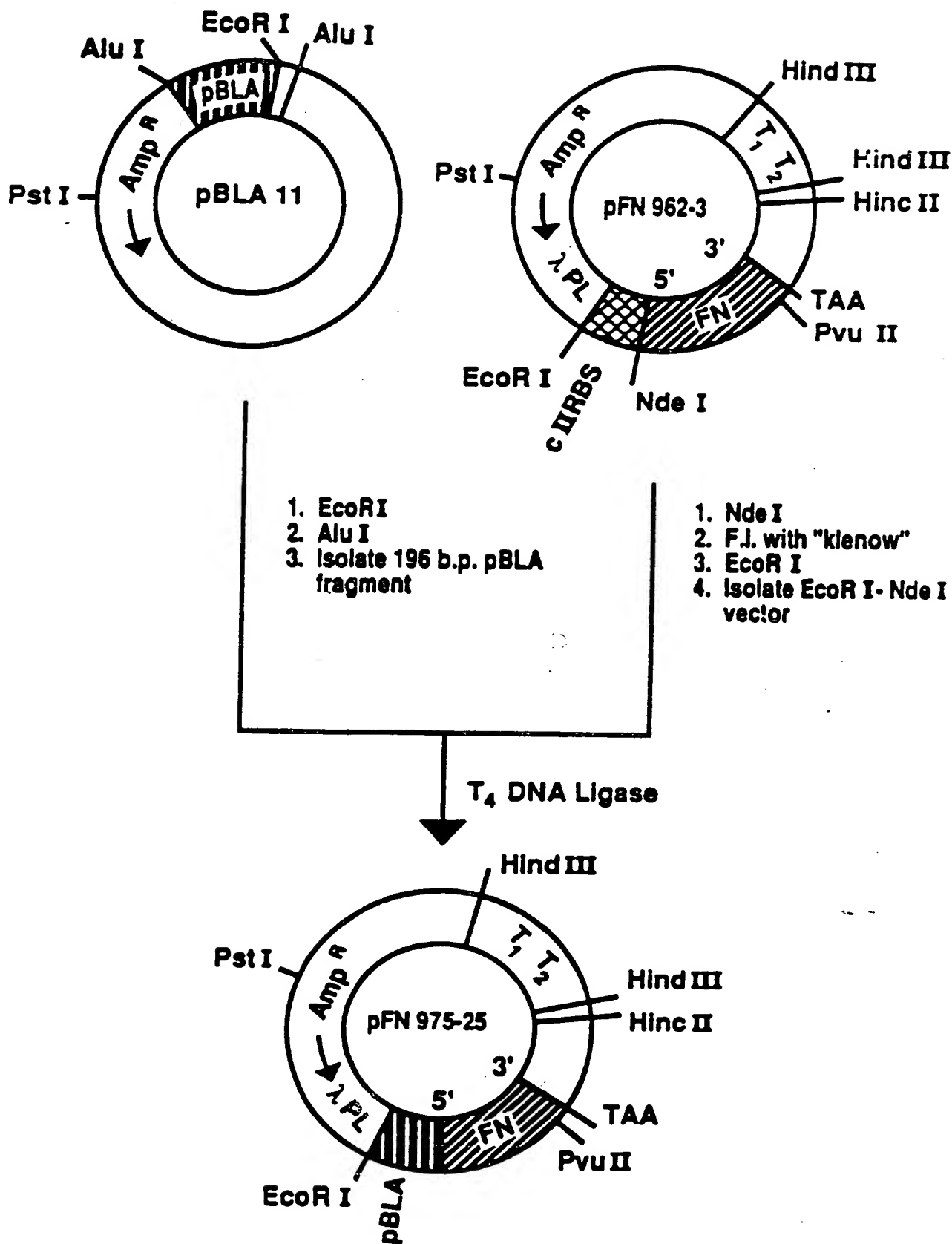


Figure 10



00462971 012700

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Figure 11

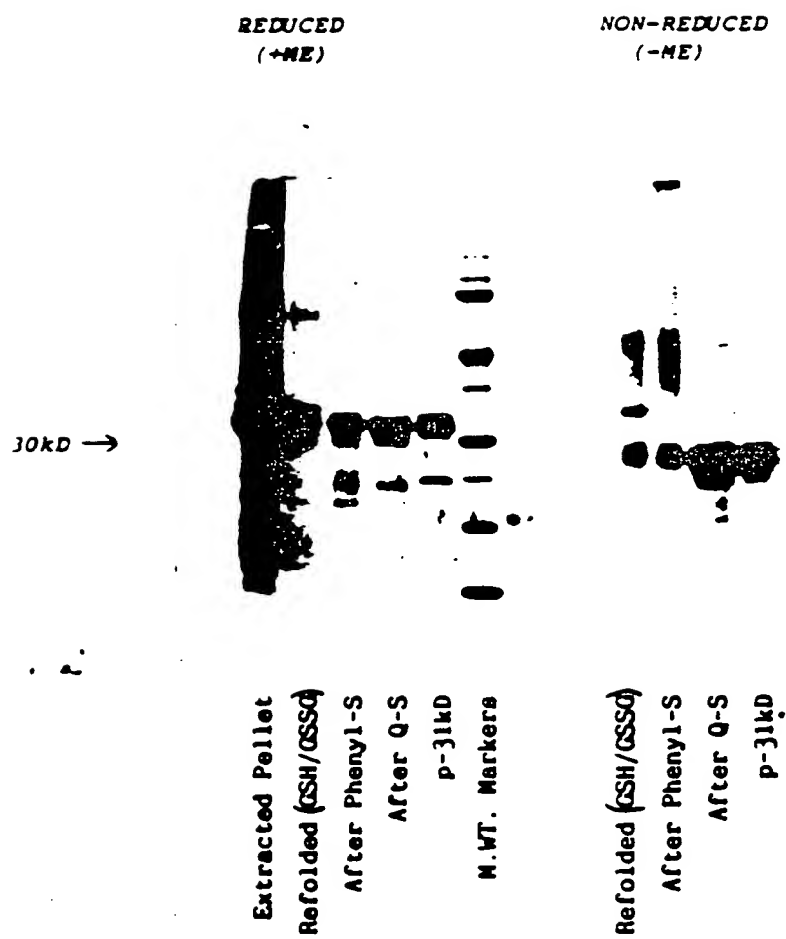


Figure 12

31kD / Phenyl-Sepharose

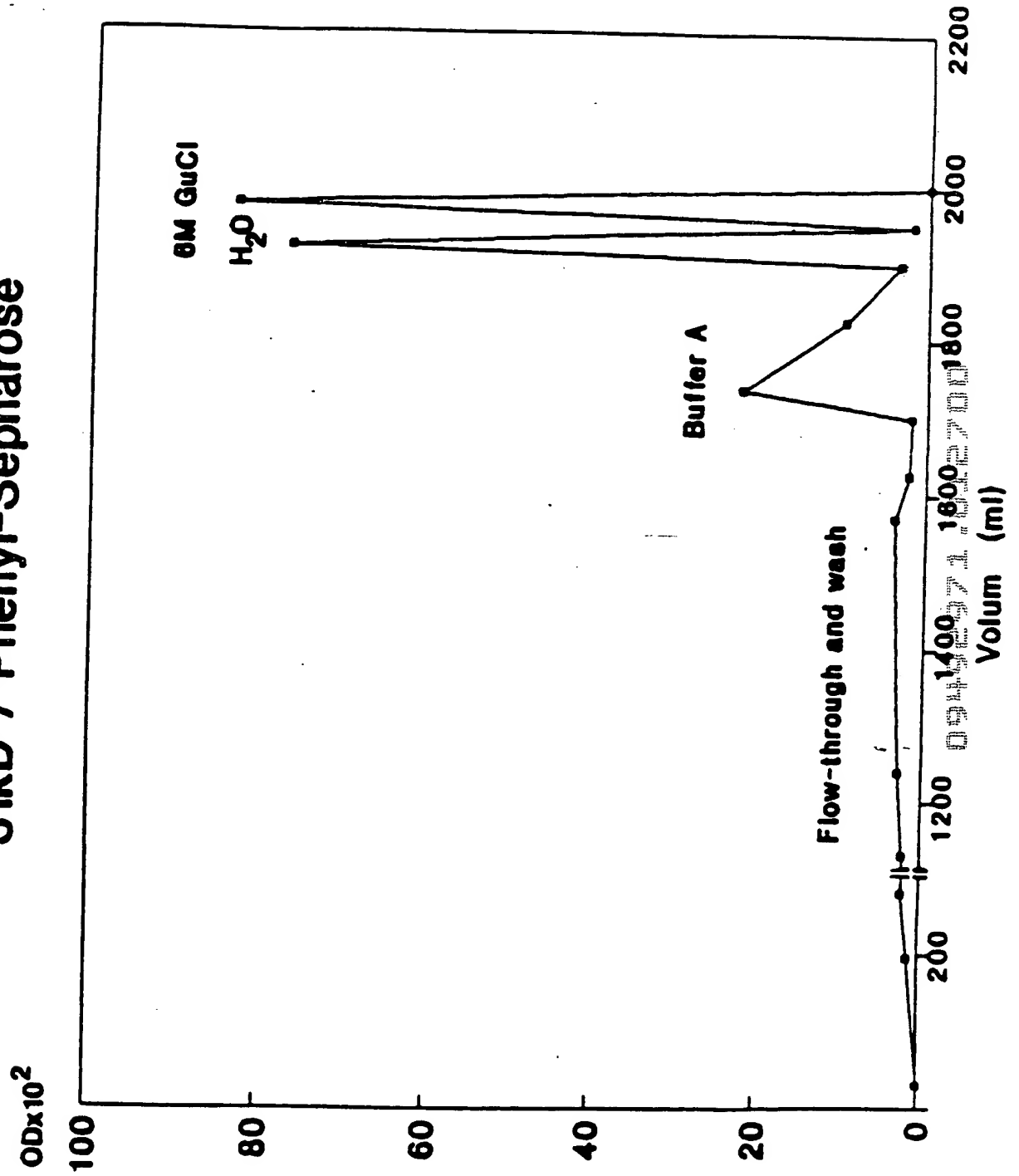


Figure 13
31kD/Heparin-Sepharose

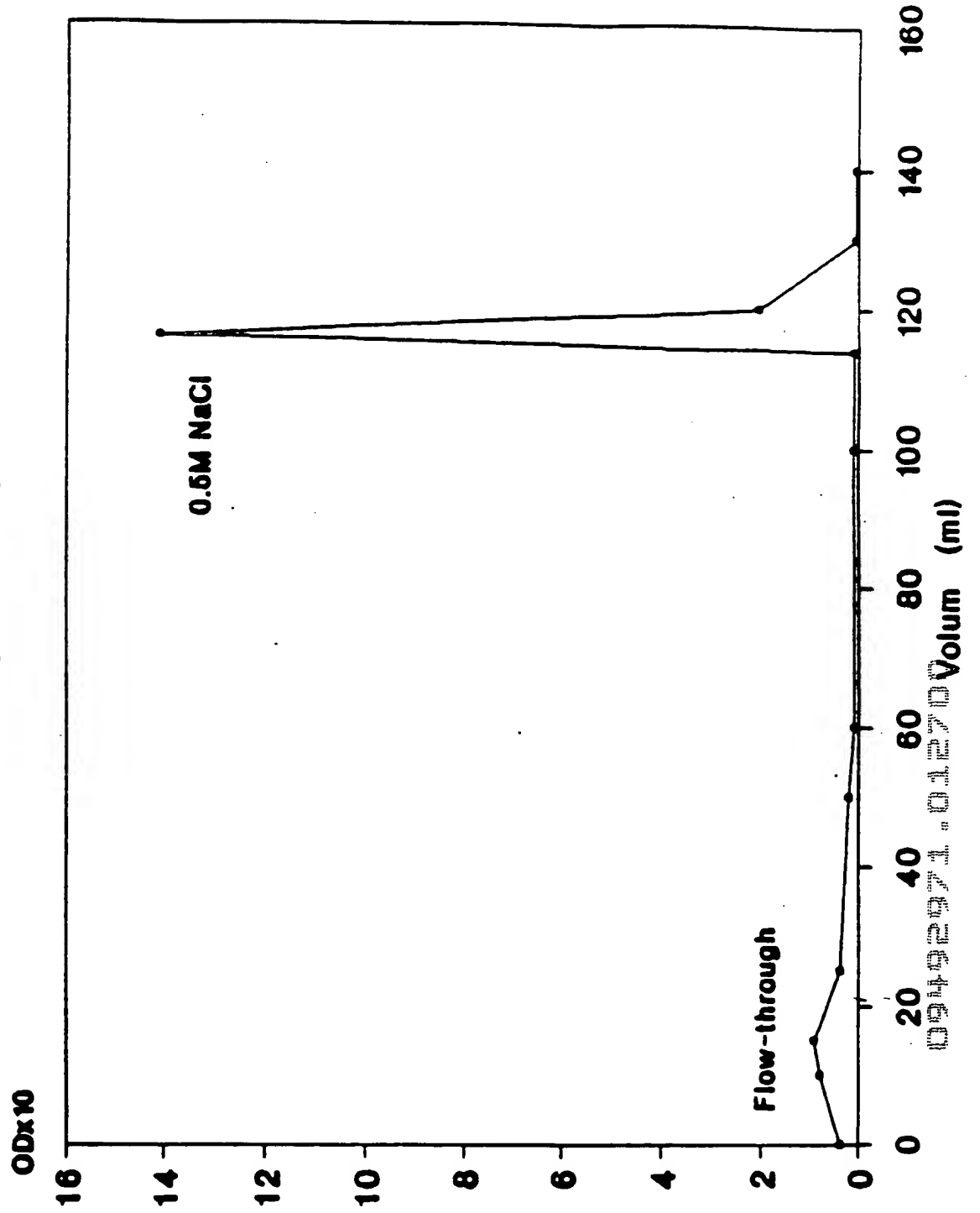


Figure 14

31kD / Q-Sepharose

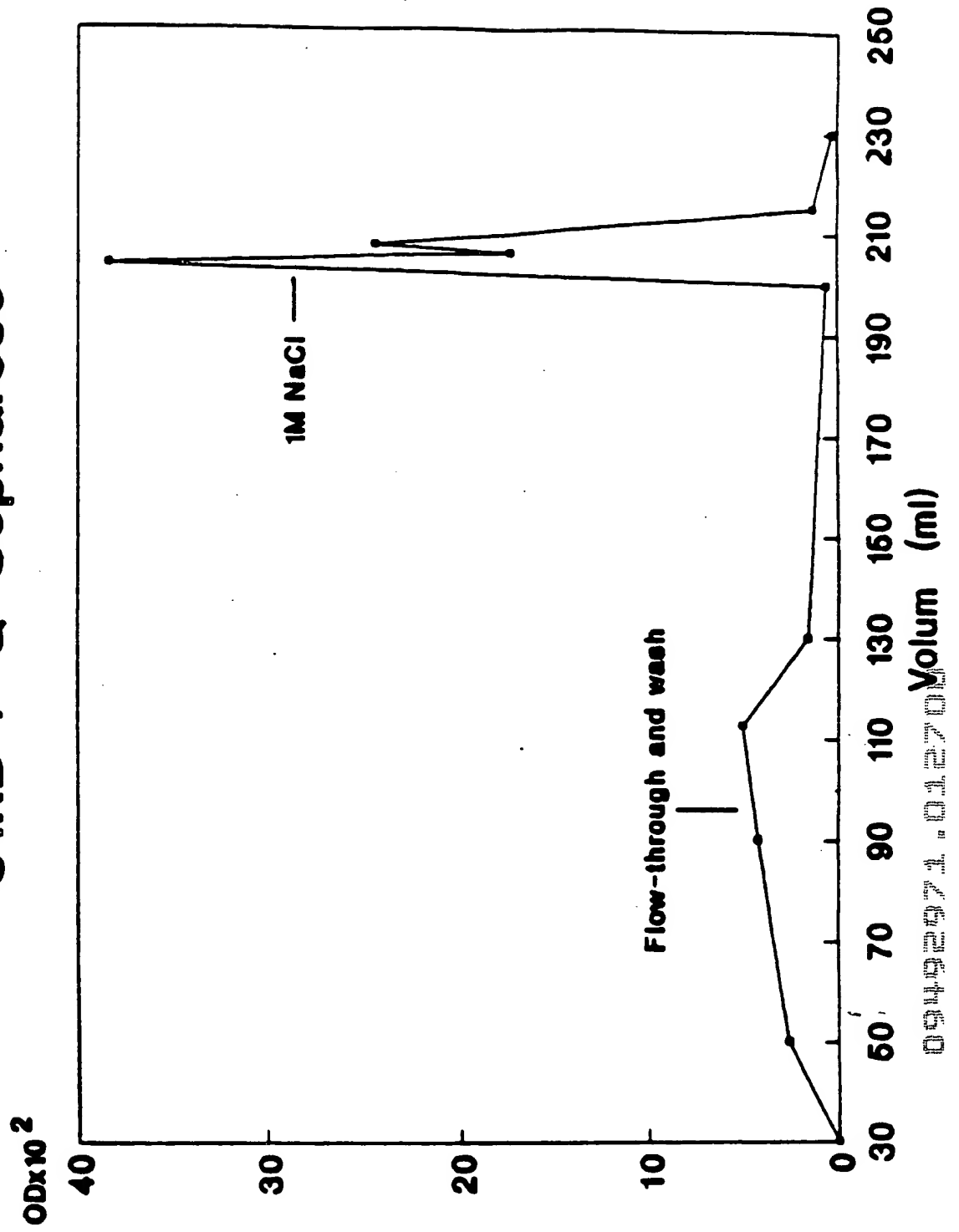
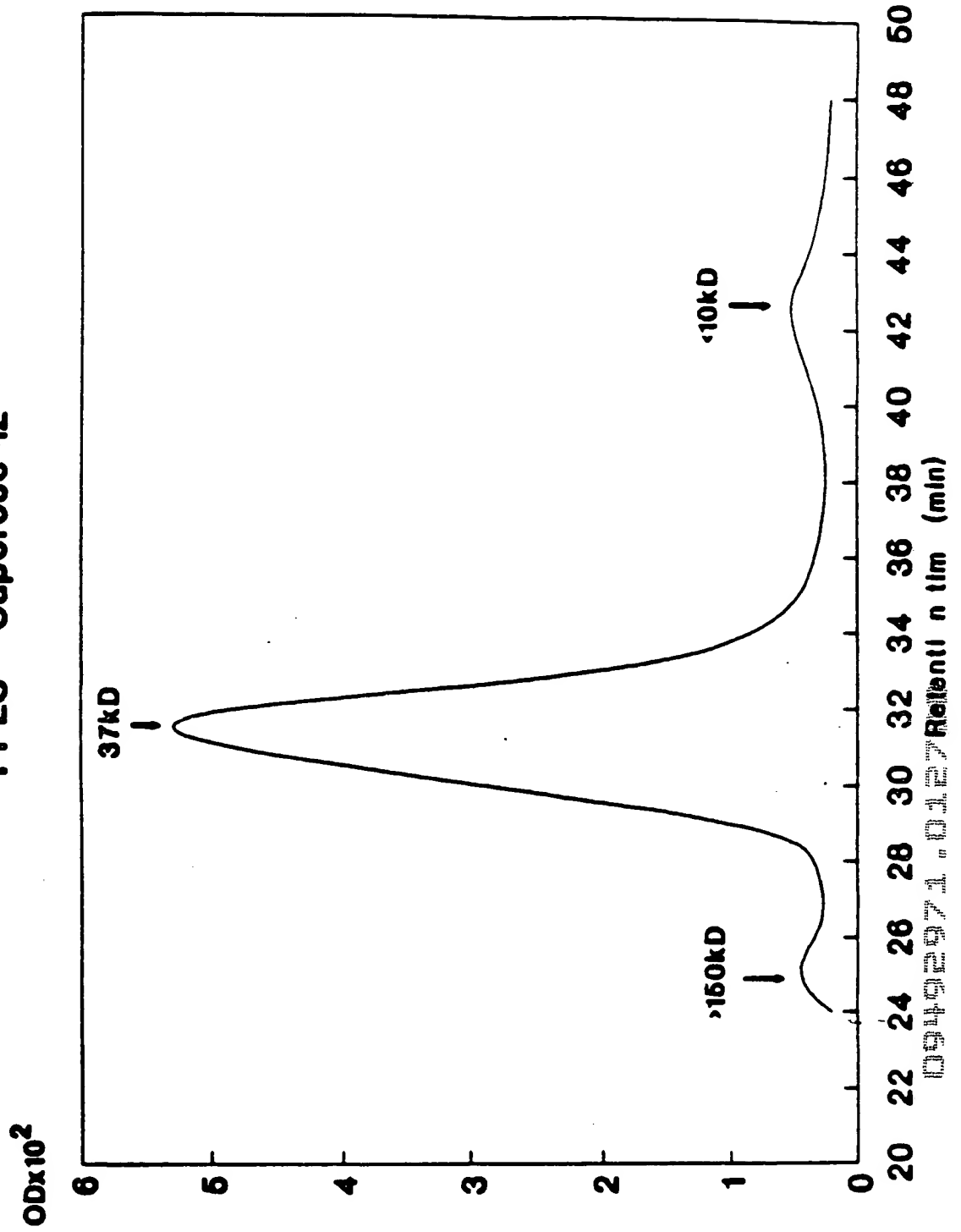


Figure 15

Mixture of rec. and plasmatic "31kD" FBD
FPLC - Superose 12



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Figure 16

Pharmacokinetic Behavior of Fibronectin
and Recombinant 31kD FBD in the Rat

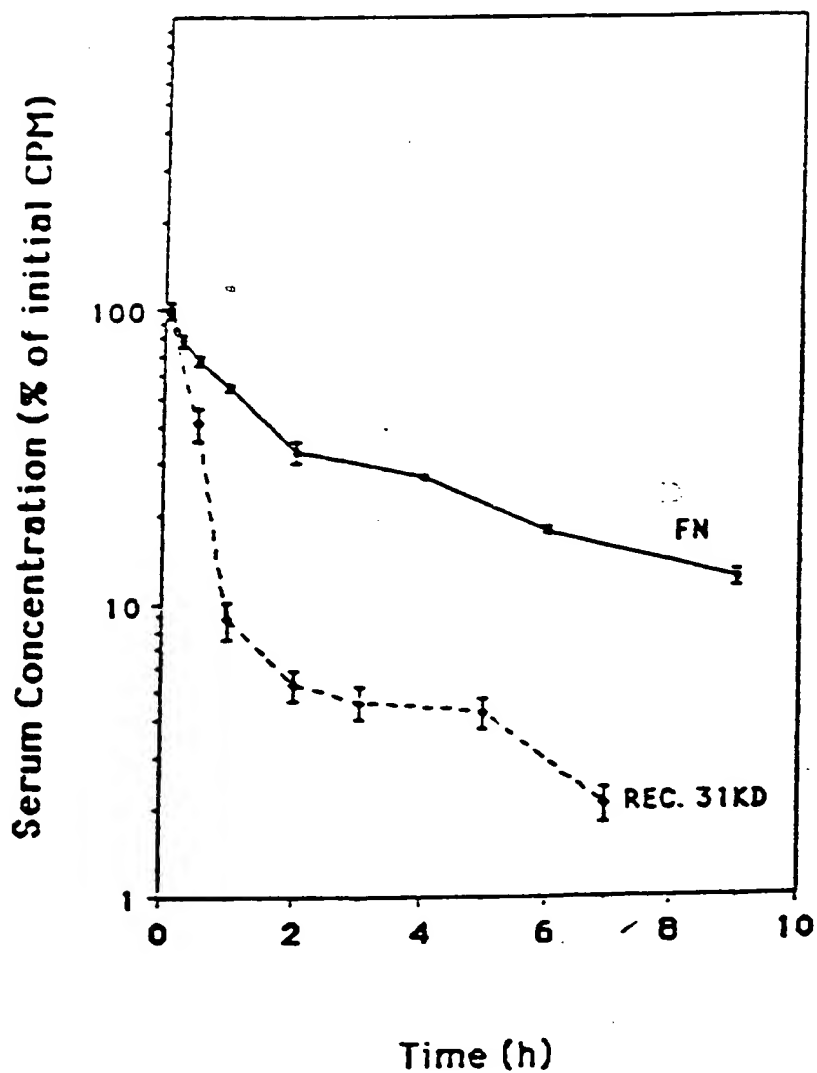
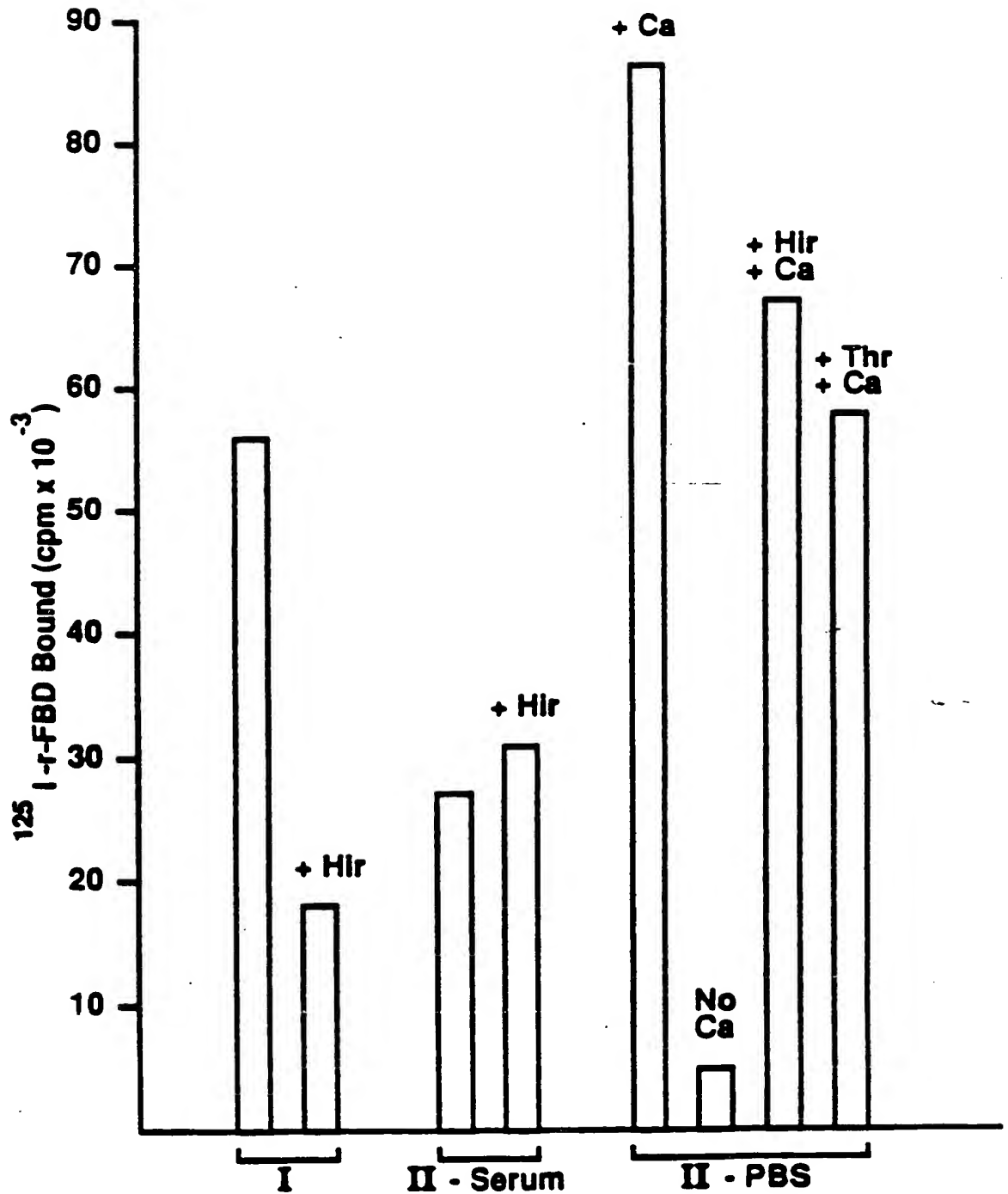


Figure 17

Binding of ^{125}I -FBD to Fibrin;
Effect of Thrombin and Ca^{++} ions.

I = Binding while clot formation

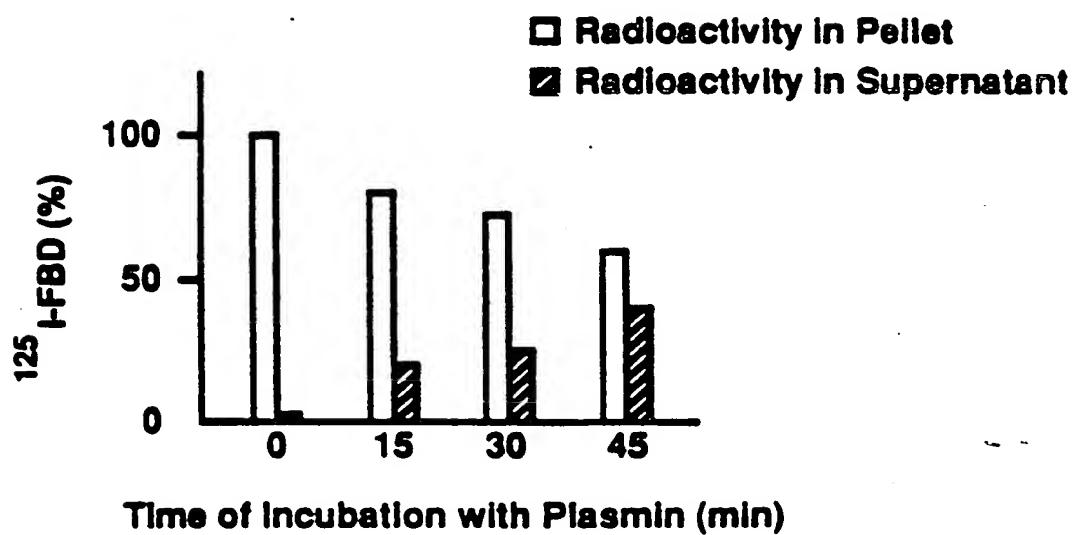
II = Binding to preformed Fibrin clot



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Figure 18

Release of 125 I-FBD from Fibrin Clot by Plasmin.



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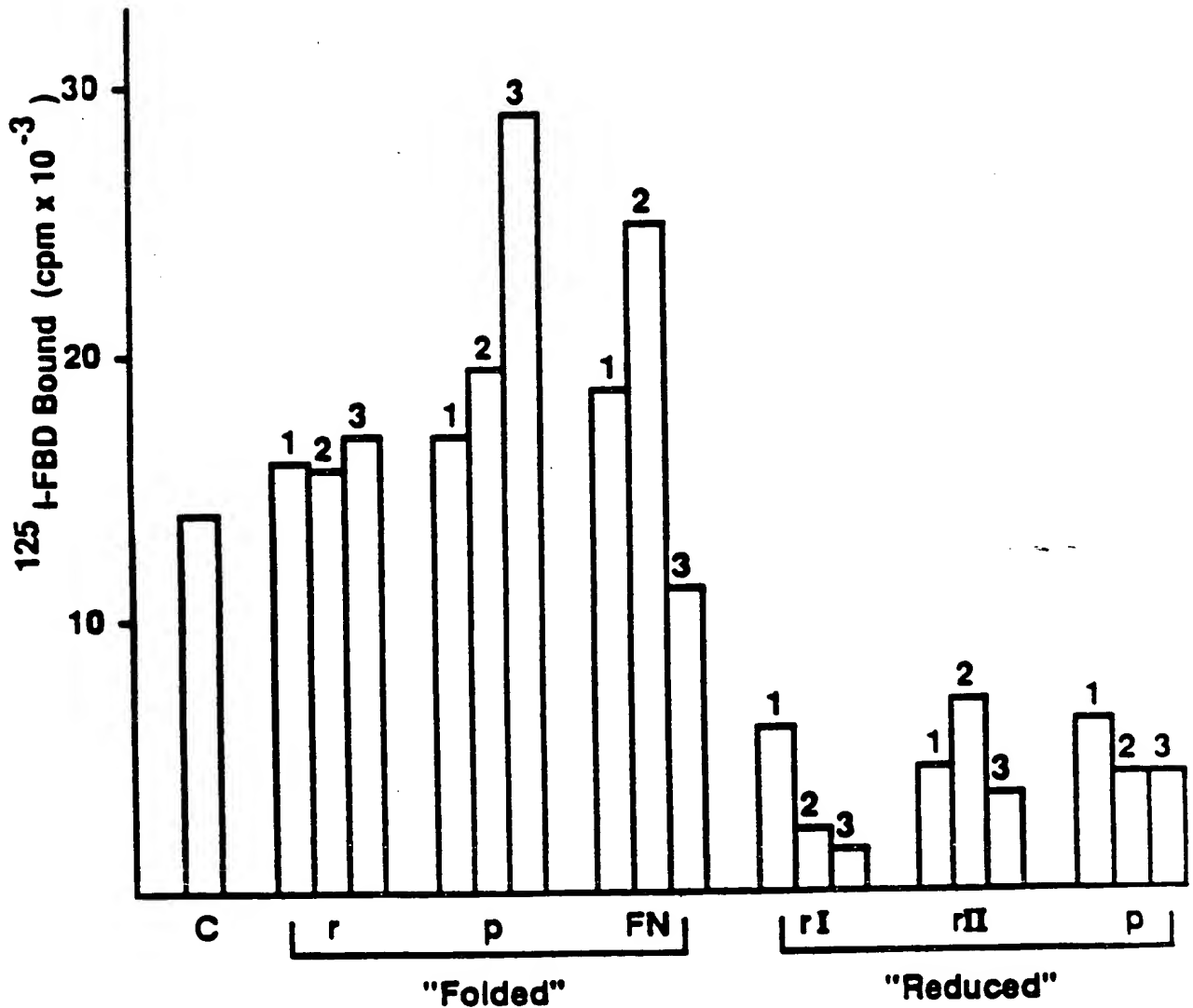
Figure 19

Binding of ^{125}I -FBD during clot formation (Reaction I) ;
Effect of unlabelled FBD and related molecules.

1 - 0.3 μM Unlabelled competitors

2 - 1.0 μM " "

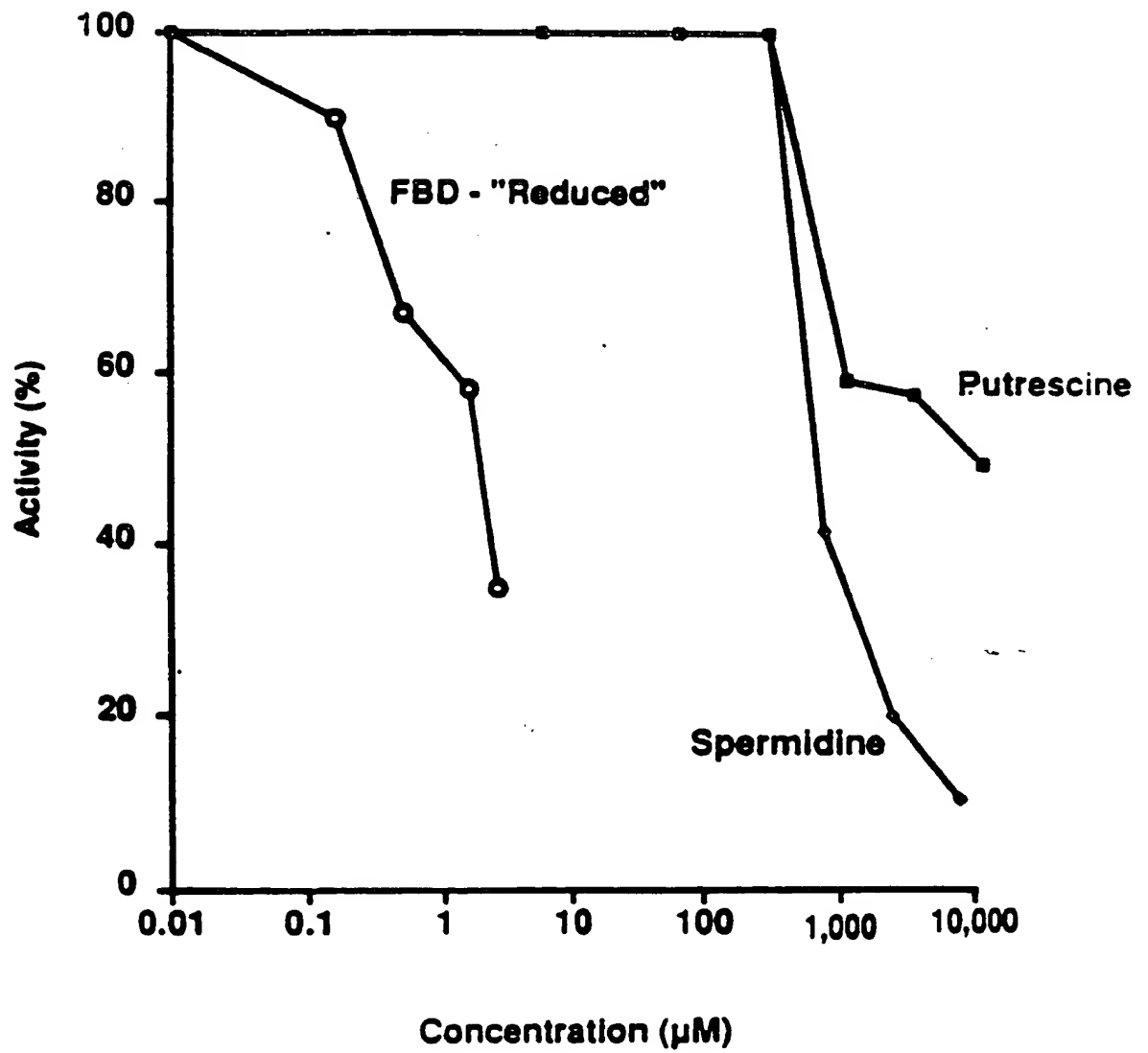
3 - 3.0 μM " "



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Figure 20

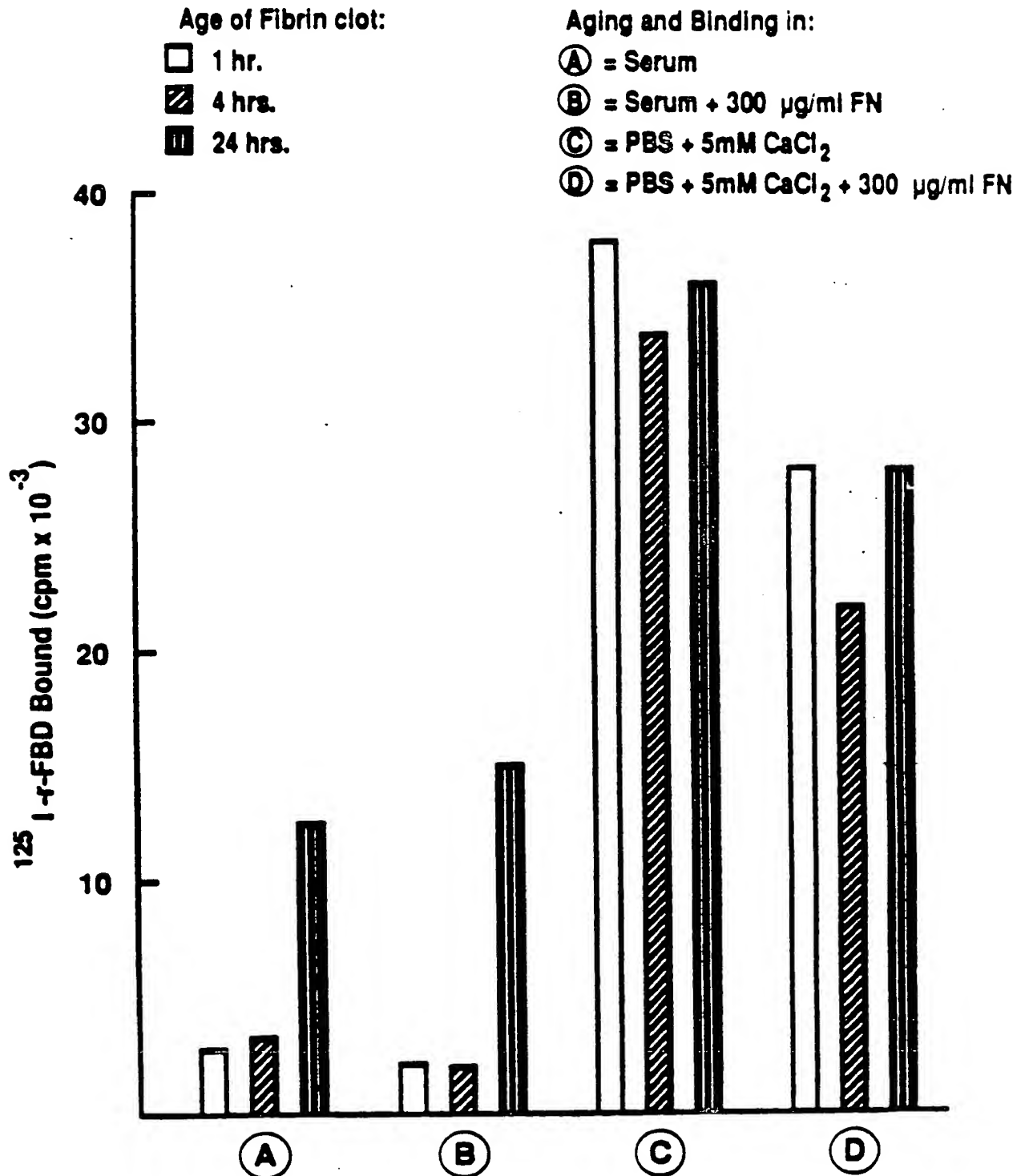
Binding of 125 I-FBD to Fibrin (Reaction II);
Effect of Transglutaminase Inhibitors.



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Figure 21

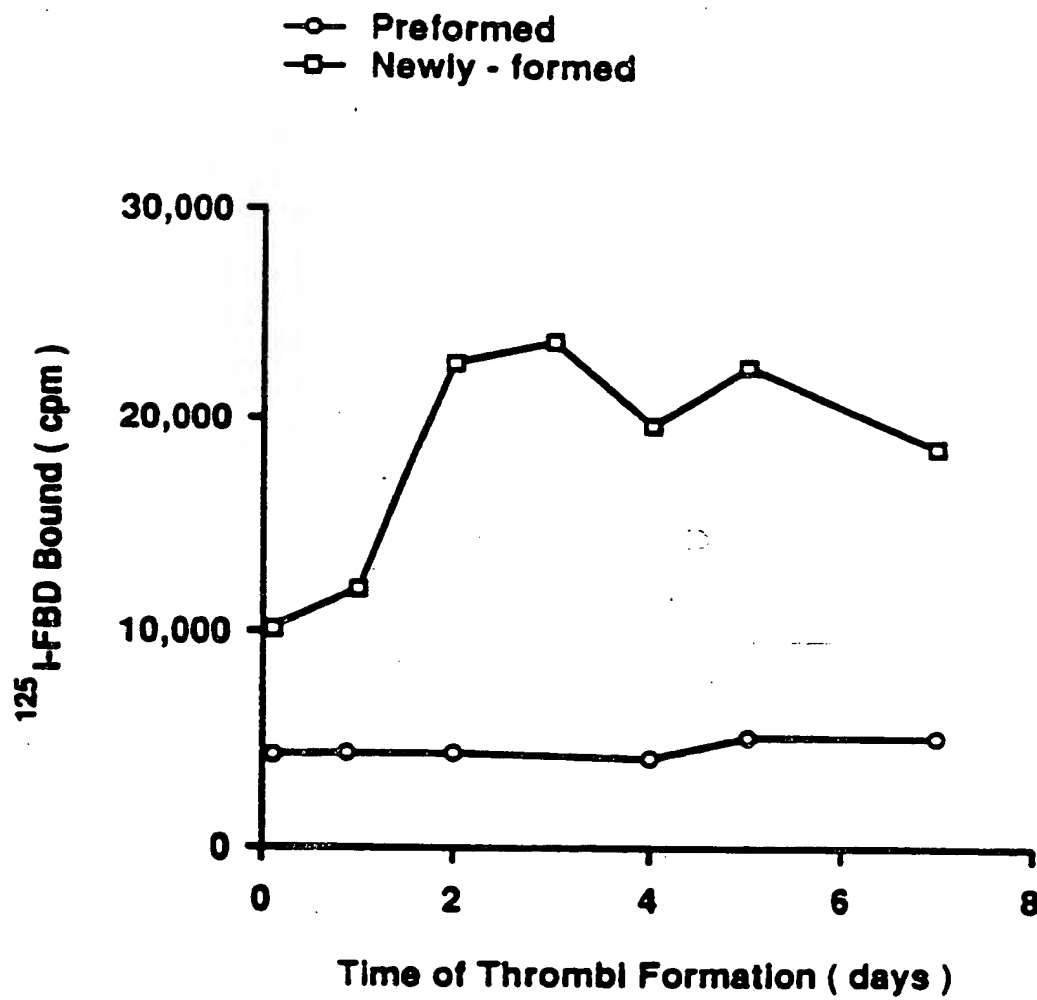
Binding of ^{125}I -FBD to preformed Fibrin clot (Reaction II);
Effect of Fibrin clot Age on the Binding (aging at 37° C).



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Figure 22

Binding of FBD to "Naive" Thrombi



Figur 23

**Binding of FBD to Fibrin (Reaction I);
Effect of Transglutaminase ("TG")
and "Reduced" - FBD**

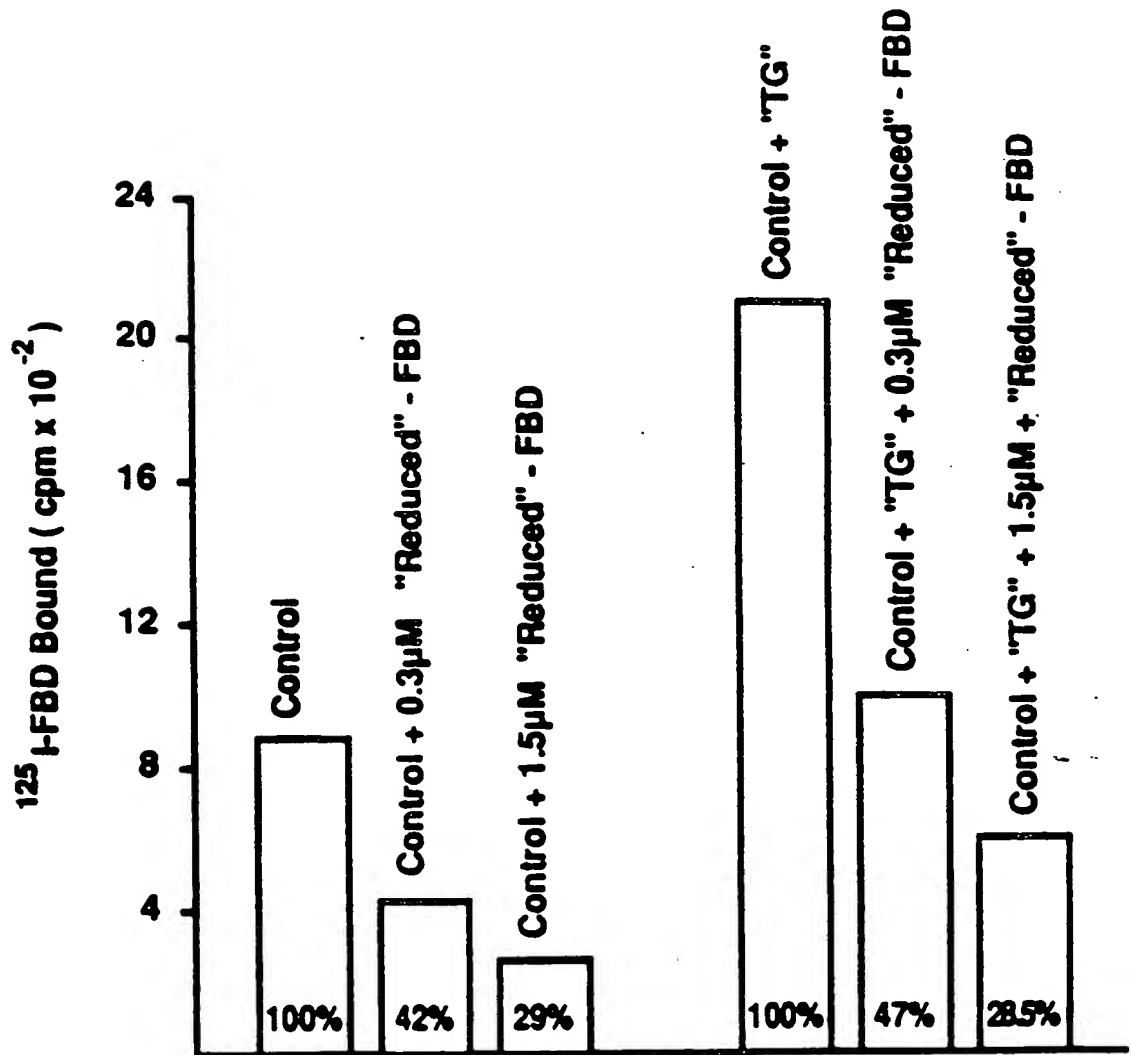


Figure 24

Binding of ^{125}I -FBD to ECM,
Effect of Ligand Concentration and Thrombin

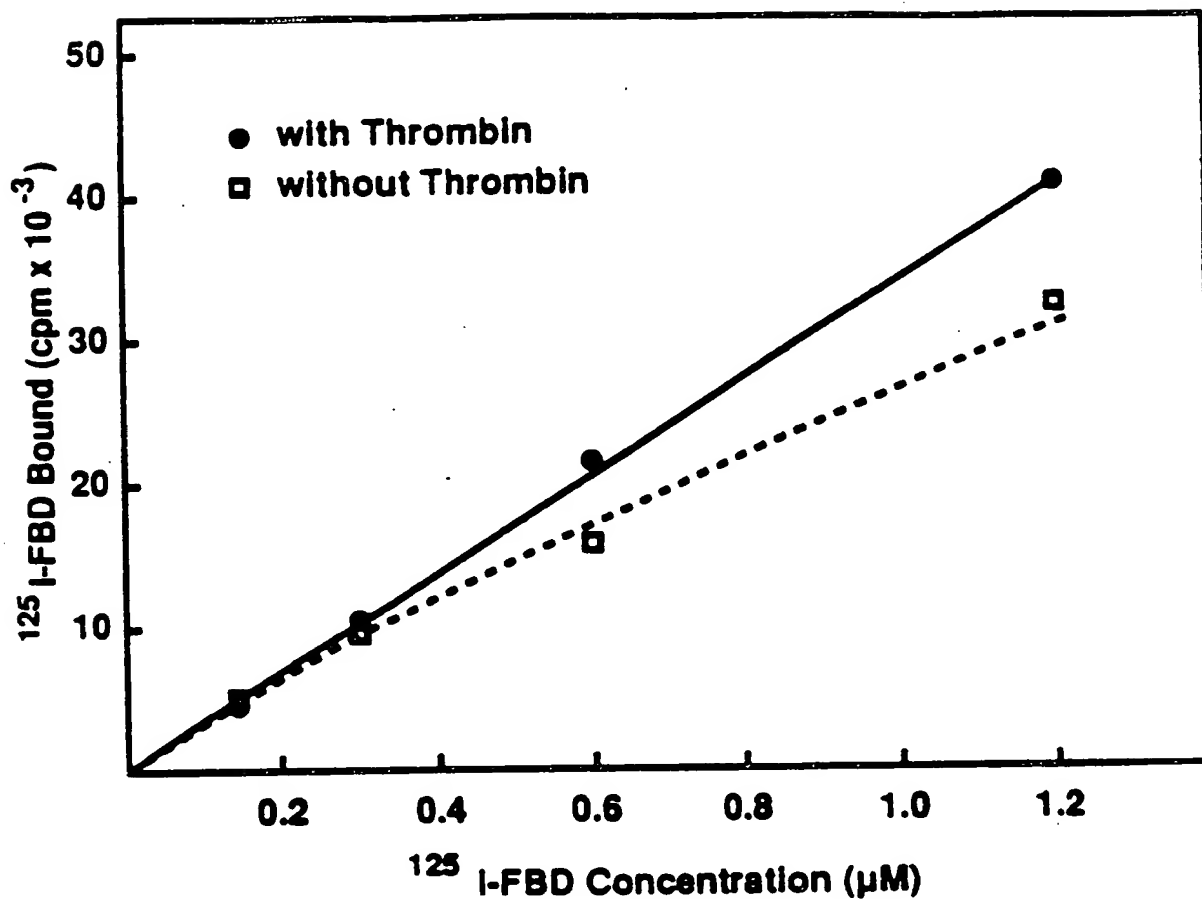
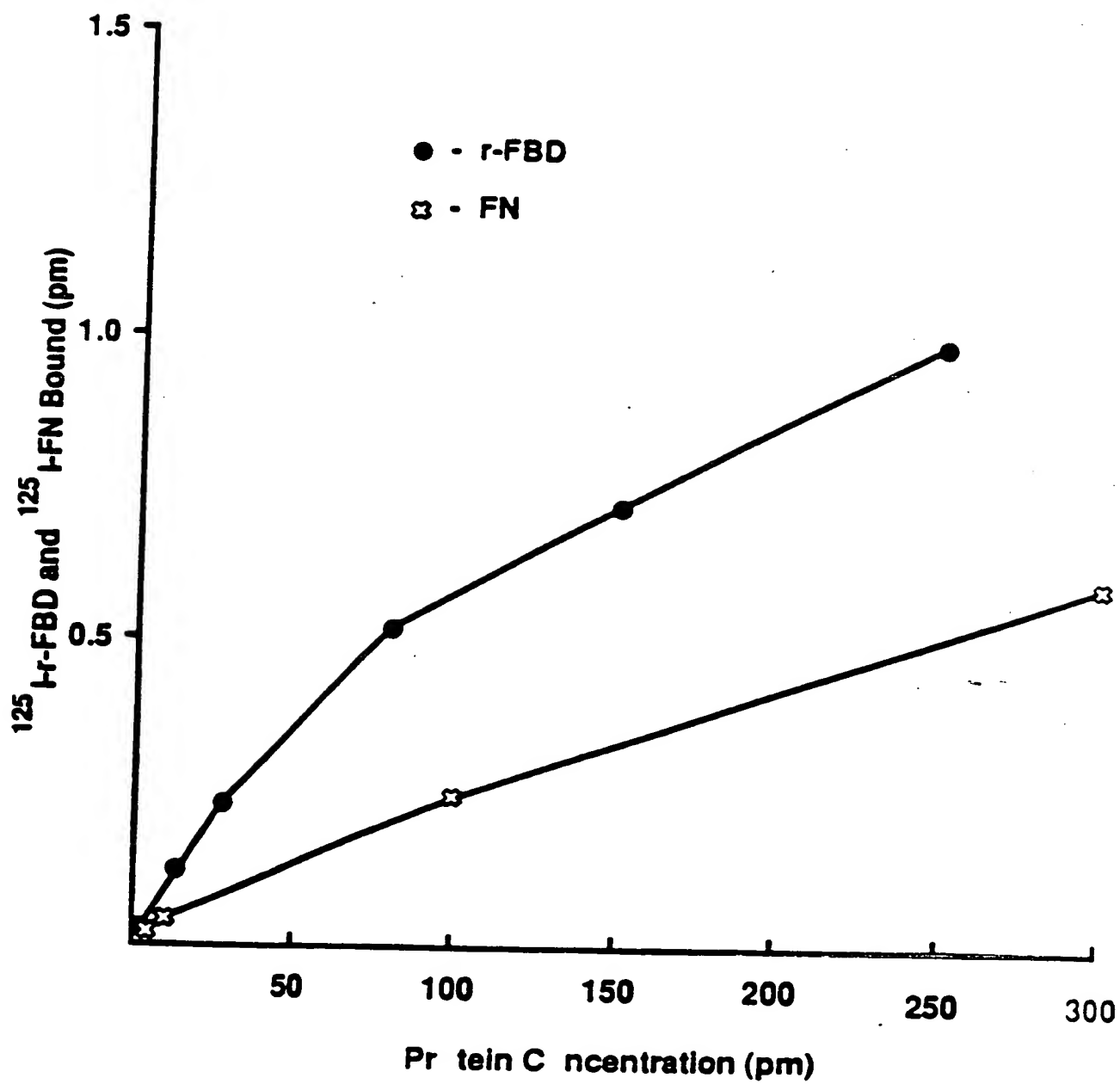


Figure 25

Binding of ^{125}I - (FN, r-FBD) to *S. aureus*



Figur 26

Binding of ^{125}I -FBD to *S. aureus*;
Competition with "Folded" and "Reduced" forms.

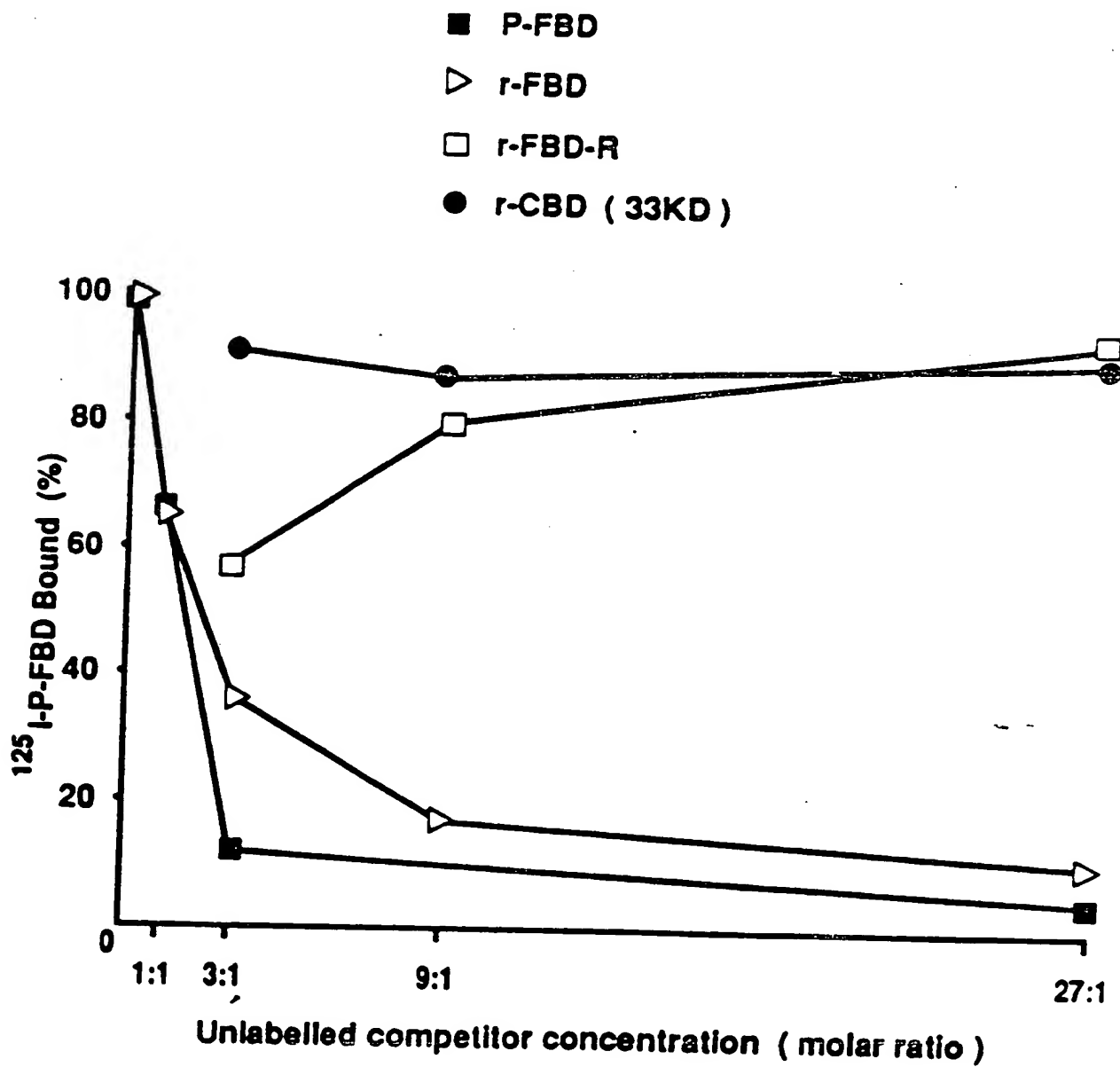


Figure 27

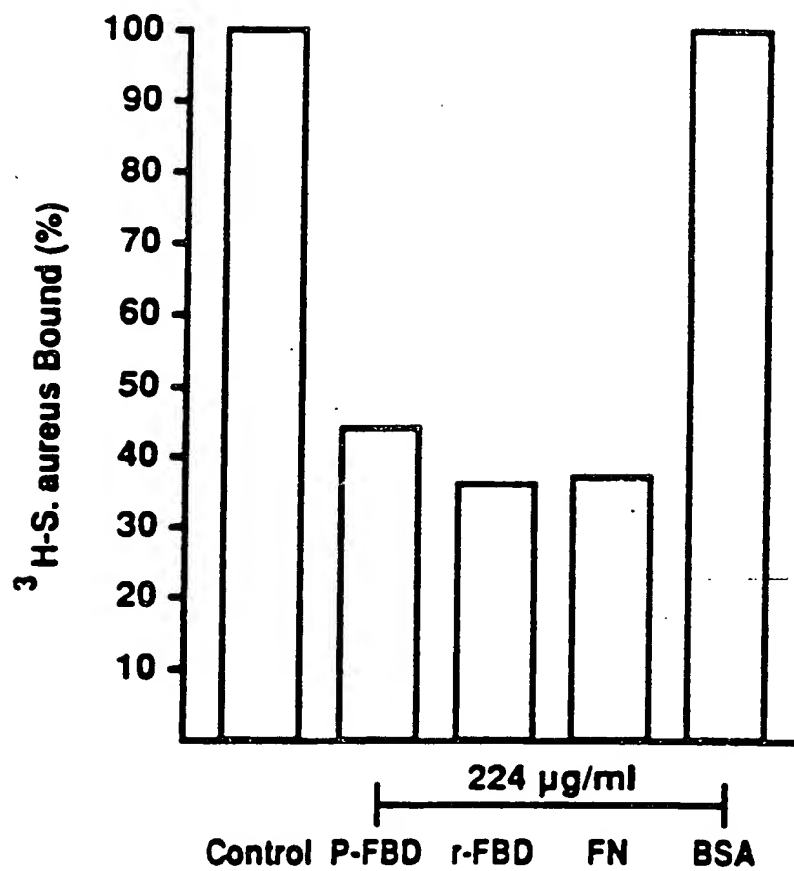
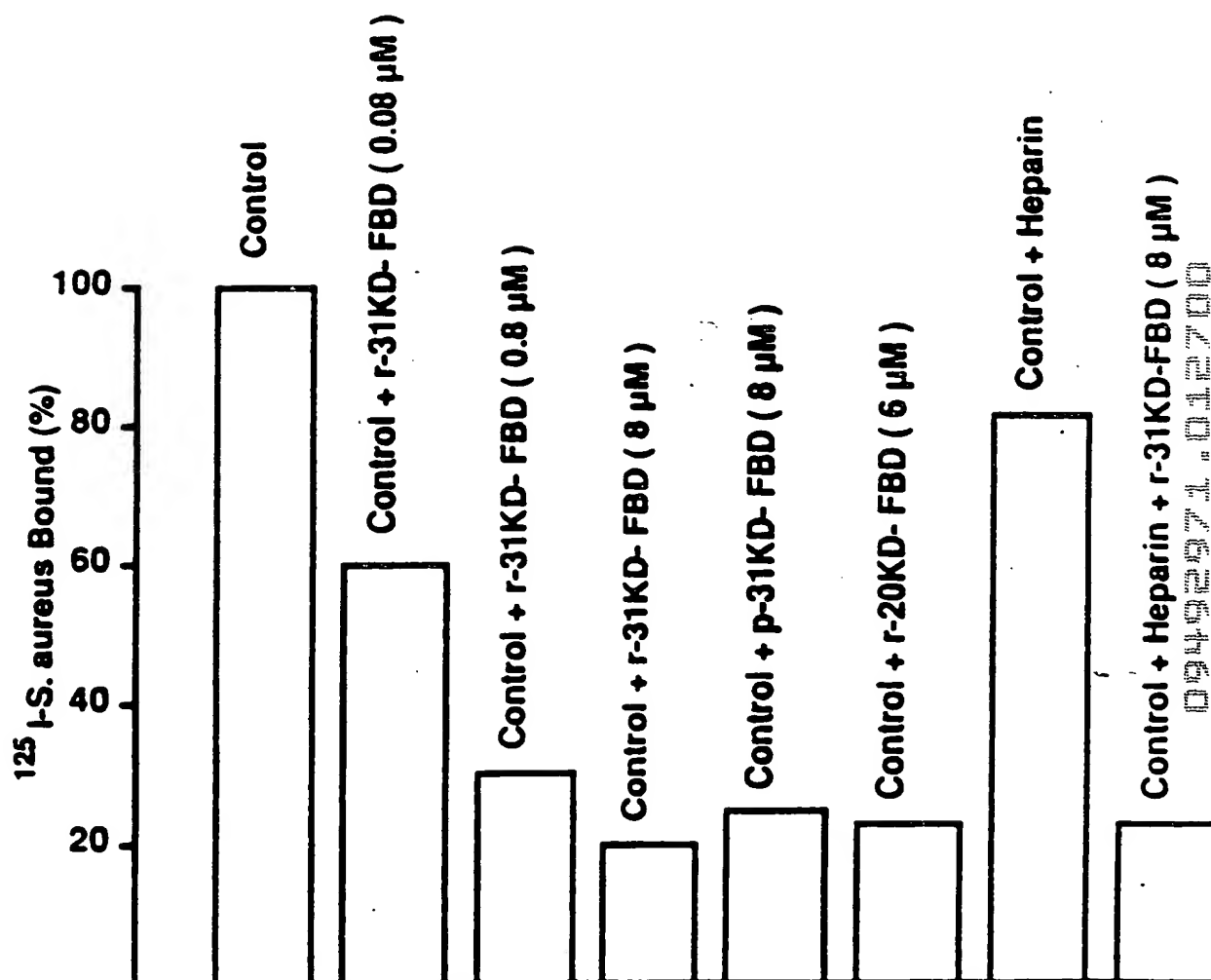
Binding of *S. aureus* to Immobilized FN.

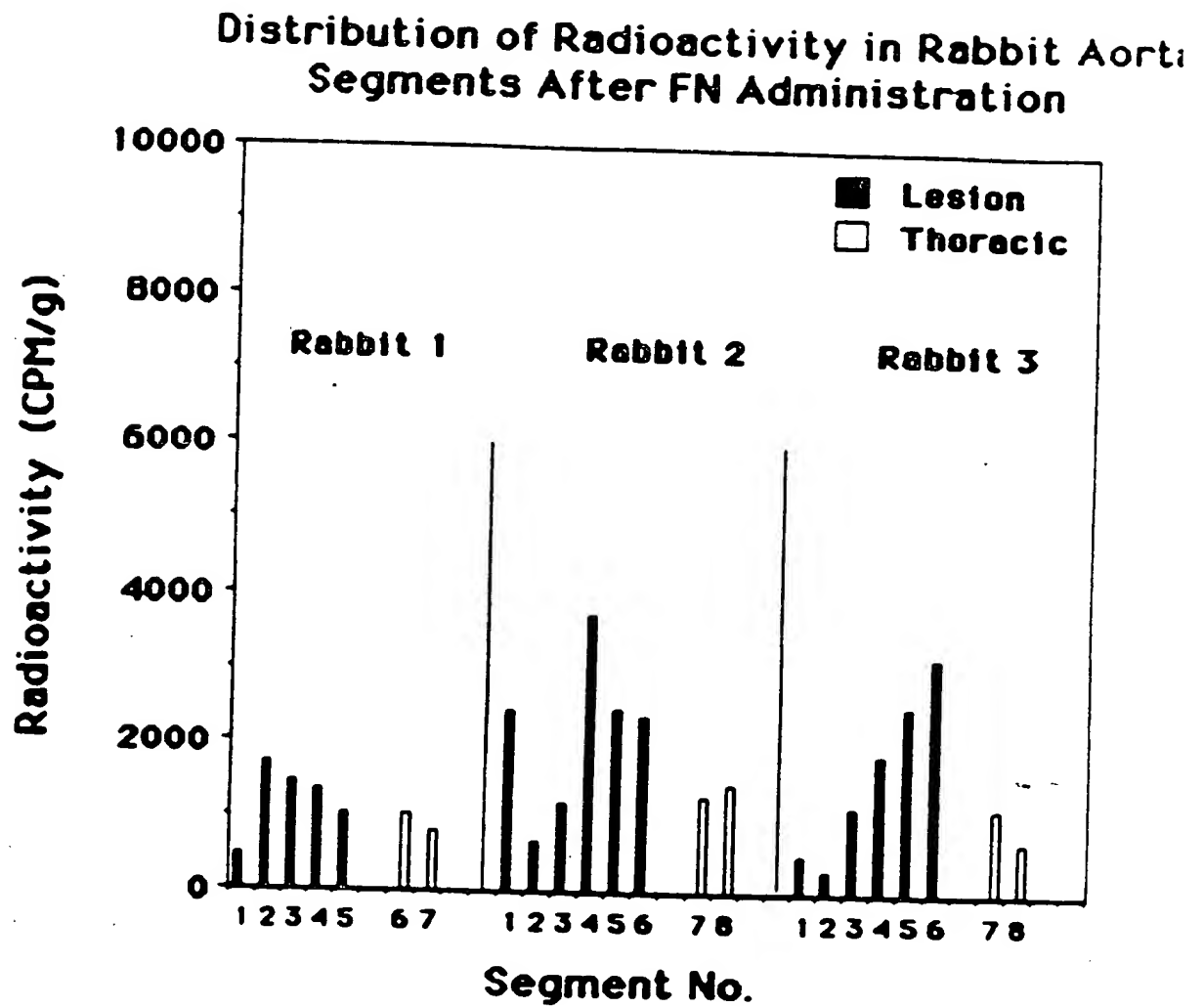
Figure 28

Binding of *S. aureus* to Bronchial Catheters;
Effect of FBD and Heparin.



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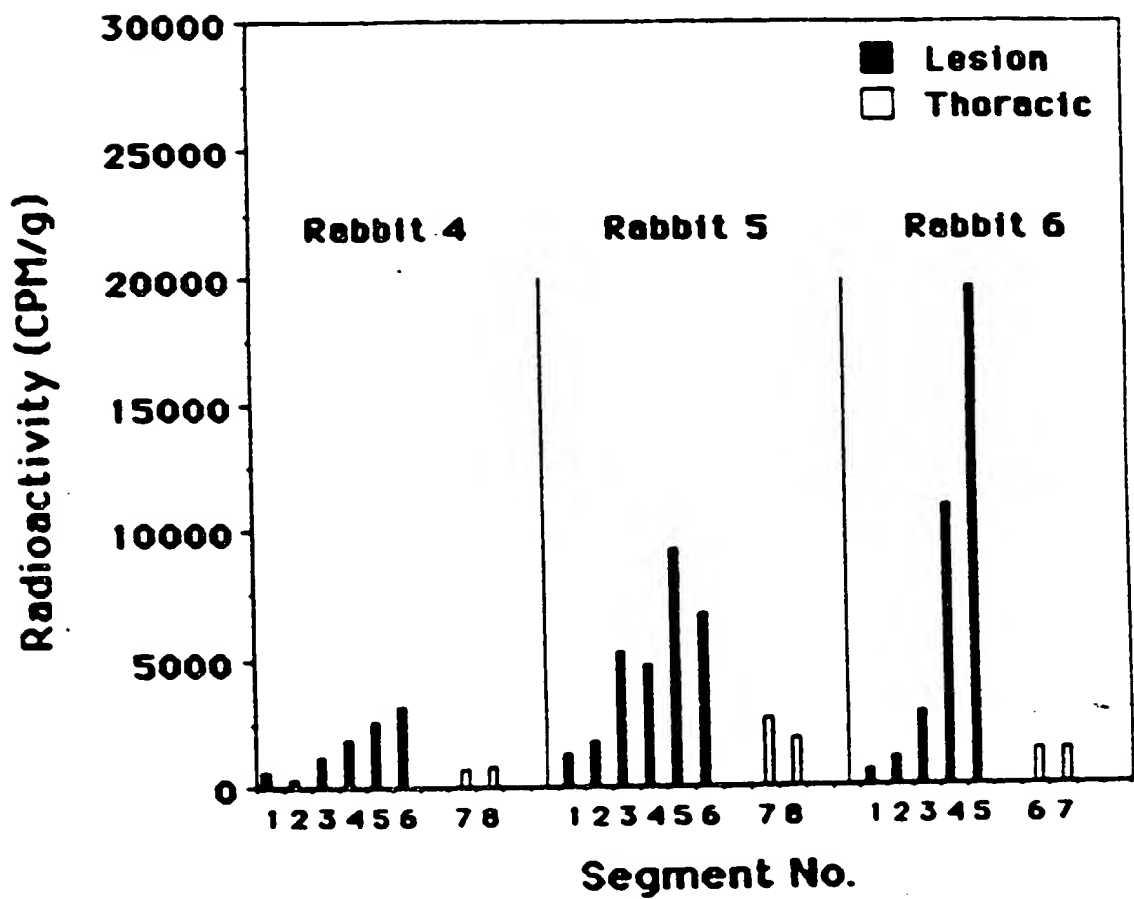
Figure 29A



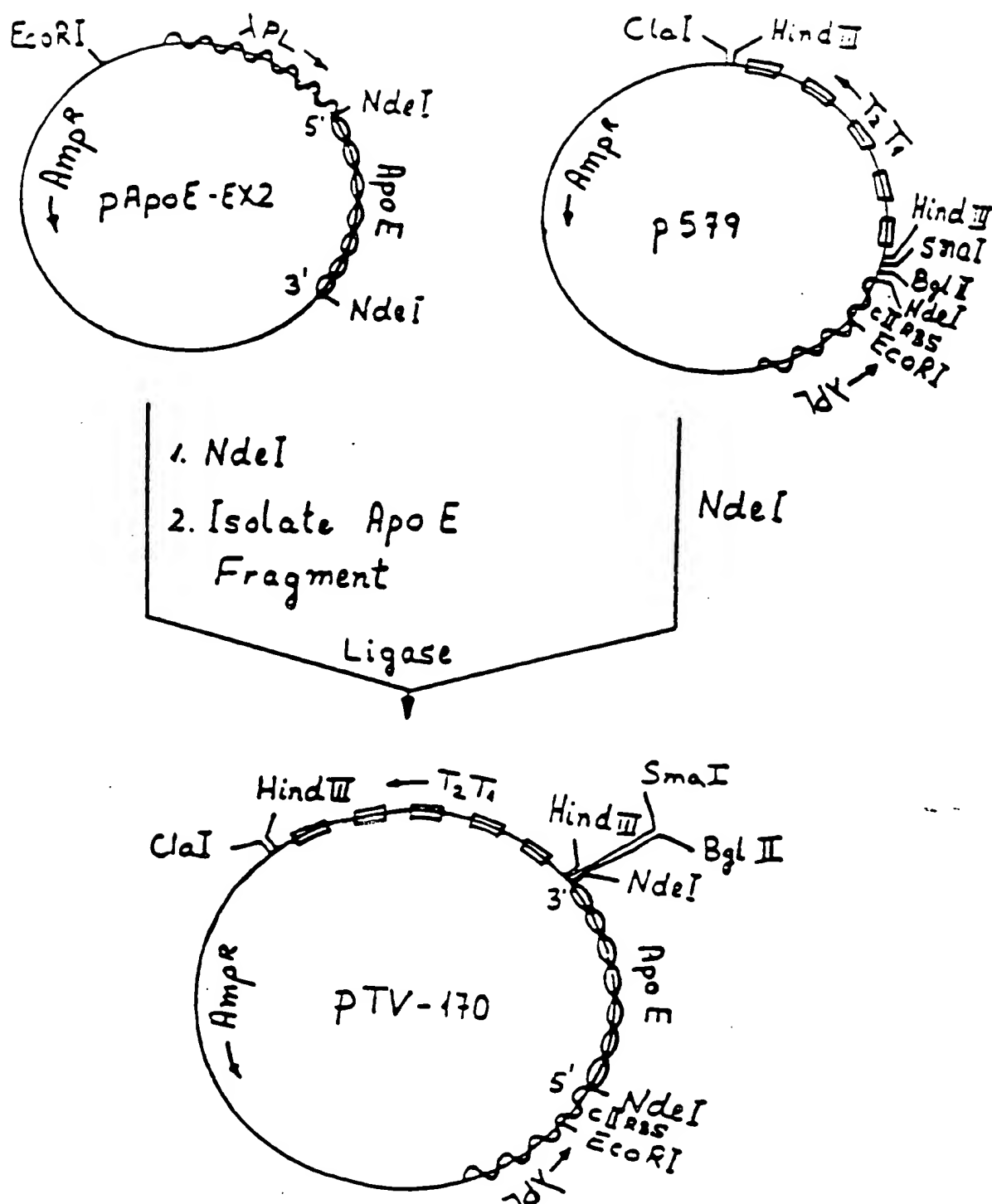
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Figure 29B

**Distribution of Radioactivity in Rabbit Aorta
Segments After 31kD FBD Administration**

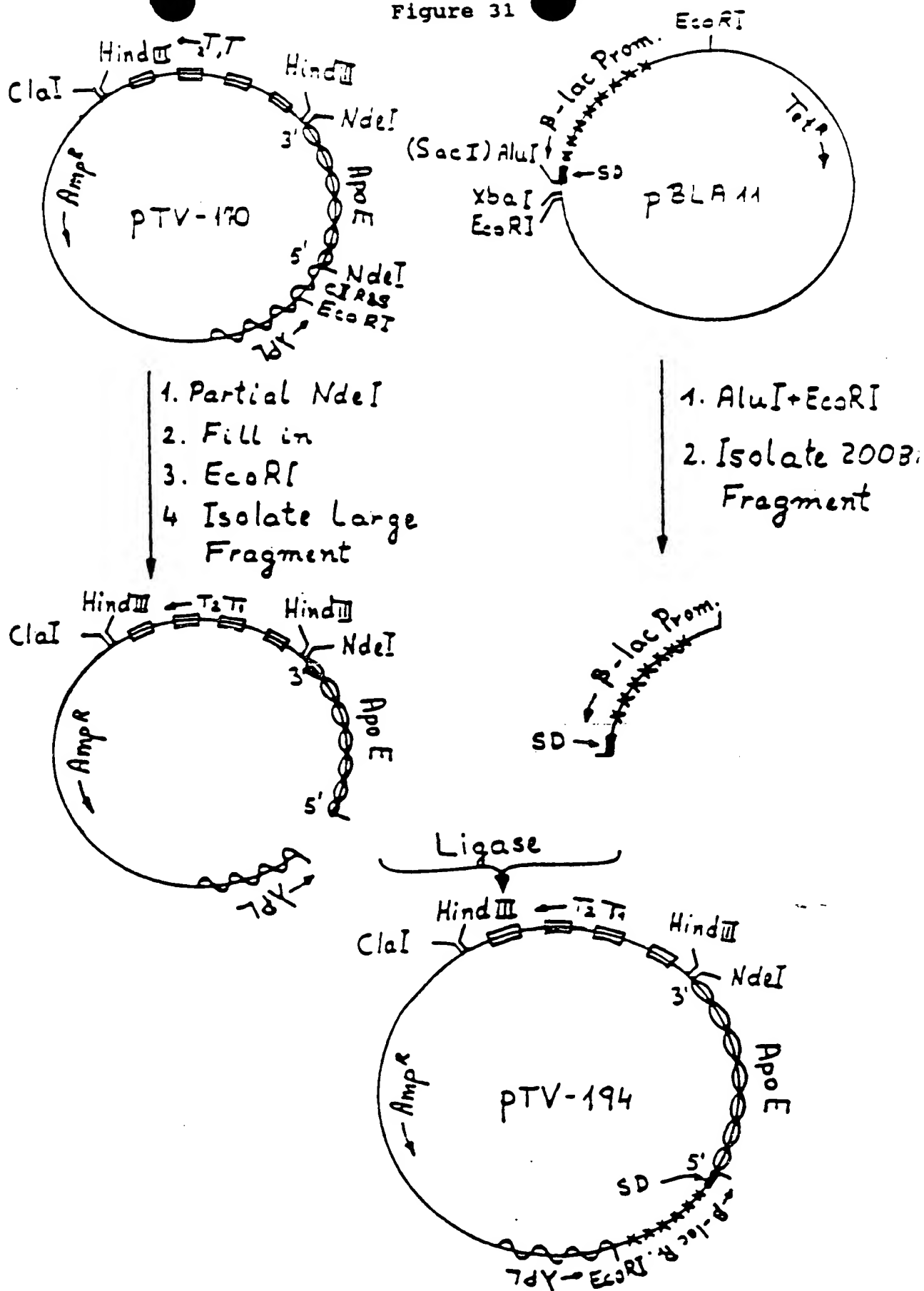


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Figure 30



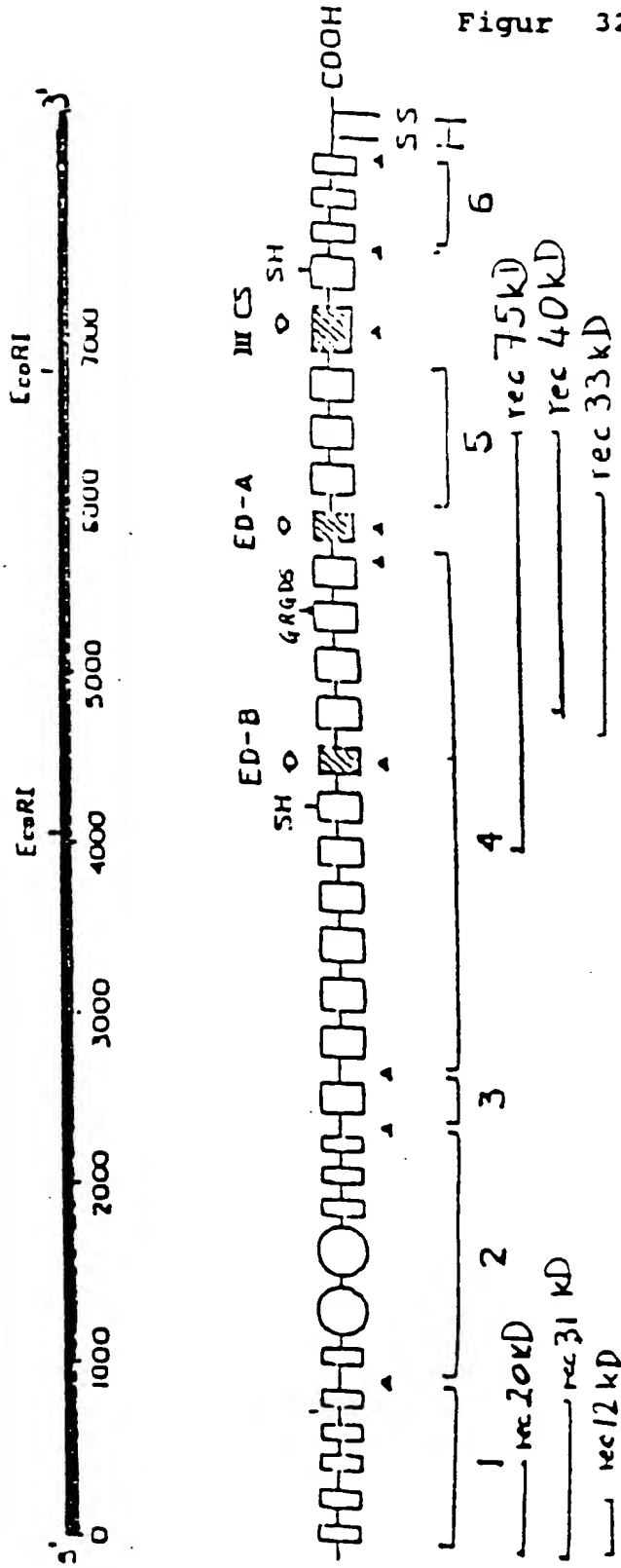
004422971.012700

Figure 31



09492571.012700

Figur 32



HEPARIN COLLAGEN [HEPARIN] CELL HEPARIN [CELL] FIBRIN
 S.AUREUS HEPARIN
 FIBRIN DNA

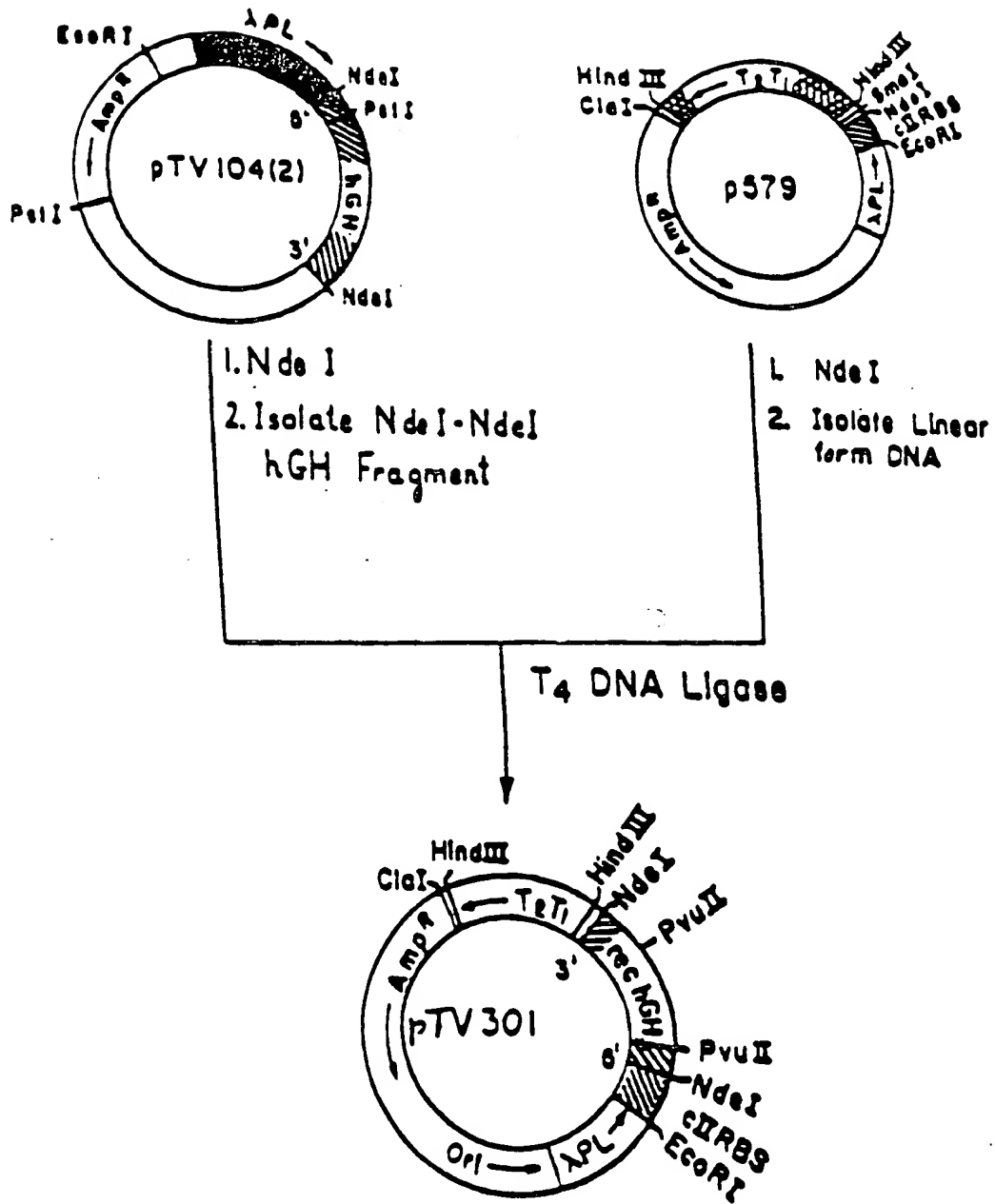
Nucleotides:

FBD	rec-12kD:	14 - 340
	rec-20kD:	14 - 472
	rec-31kD:	14 - 799
CBD	rec-40kD:	4251-5566
	rec-75kD:	2317-5566
	rec-33kD:	3498-5179

09492971-012700

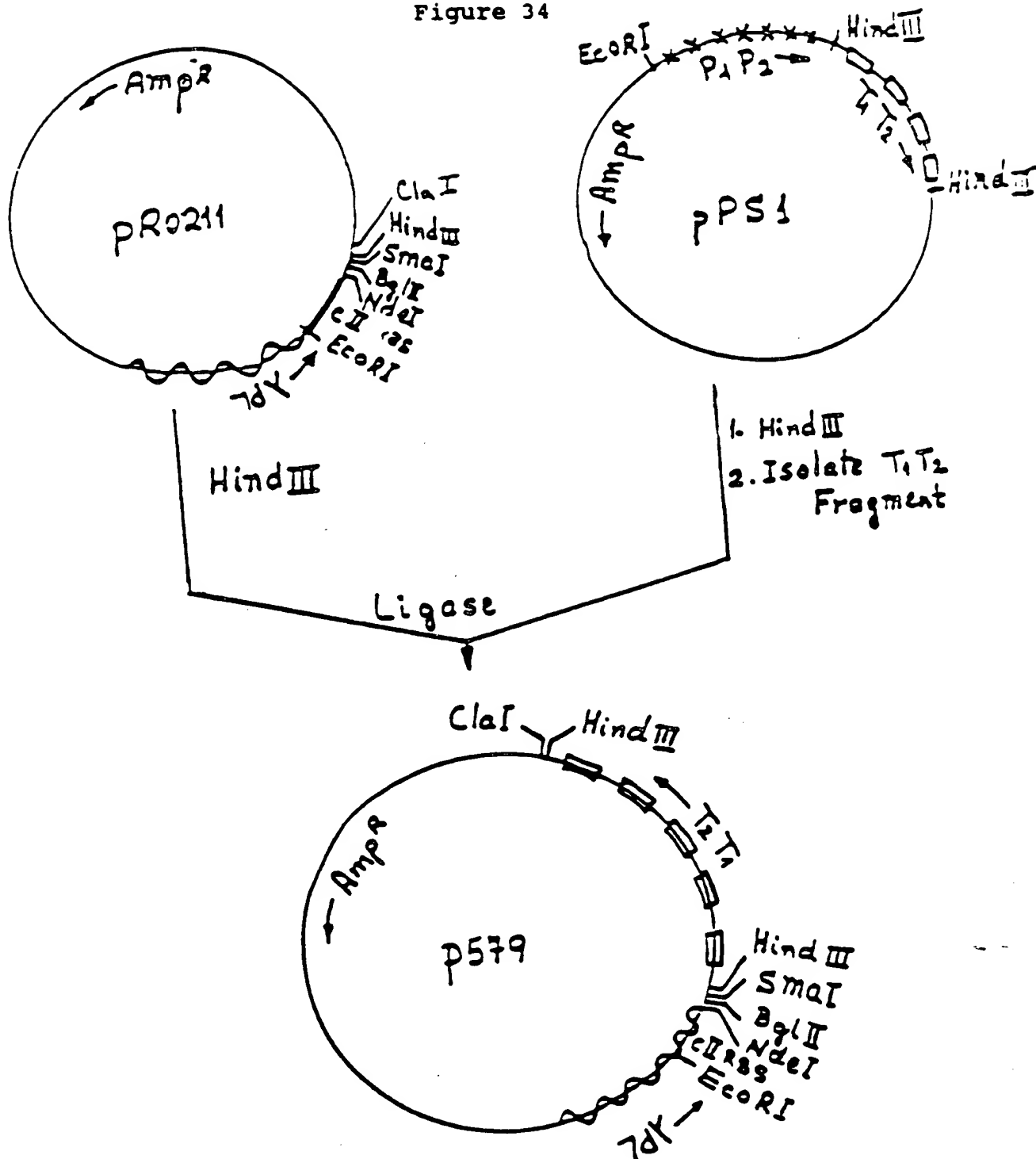
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Figur 33



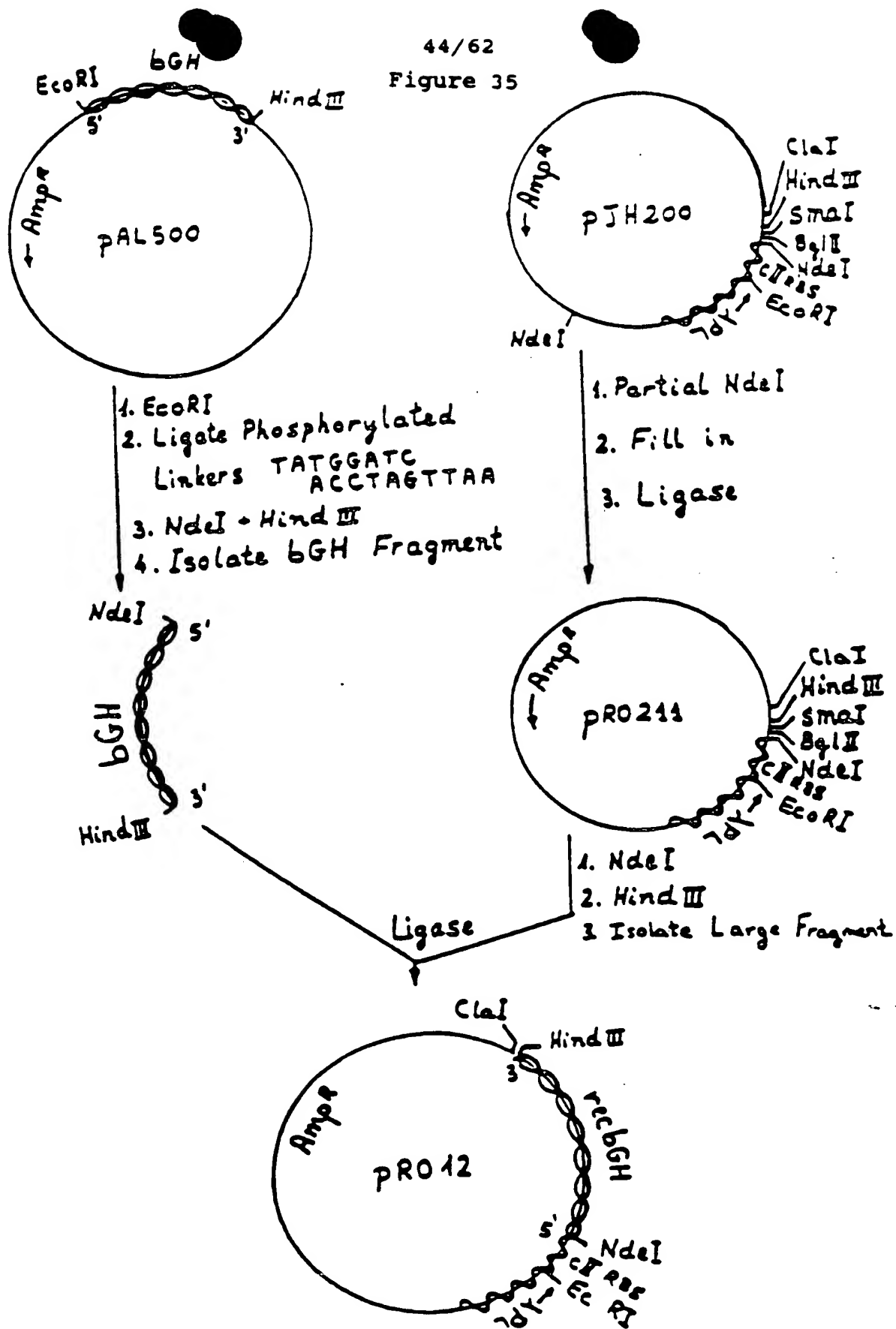
002210" T 2525160

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Figure 34



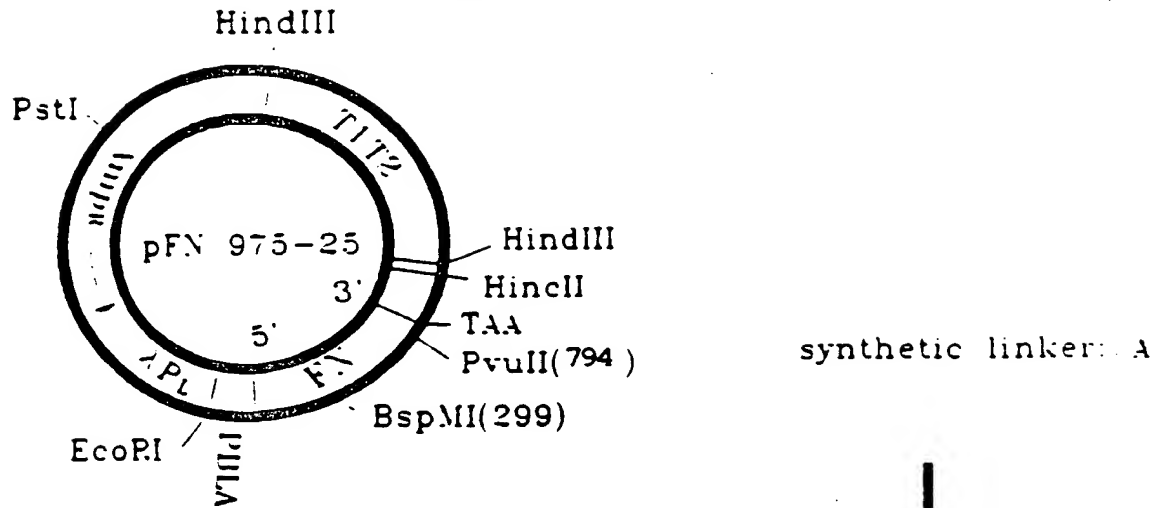
002210-12525460

Figure 35



00492971.013700

Figur 36



1. digest with BspMI+HindIII
2. isolate large BspMI-HindIII fragment

T4 DNA ligase

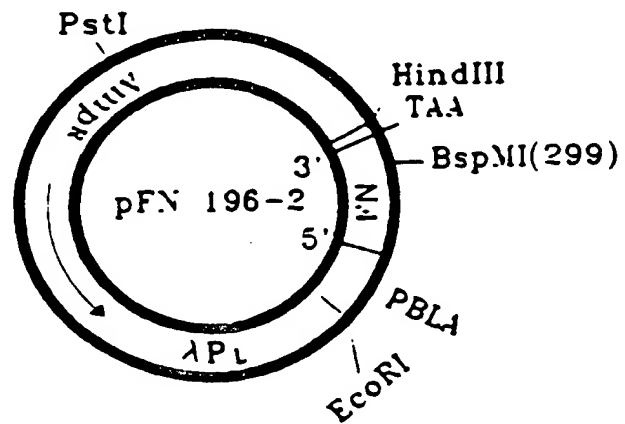
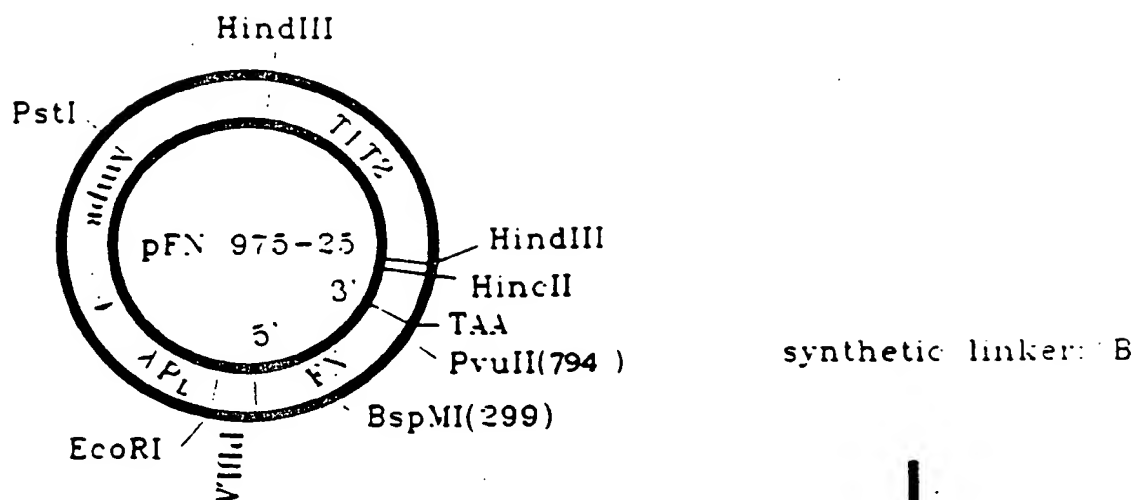
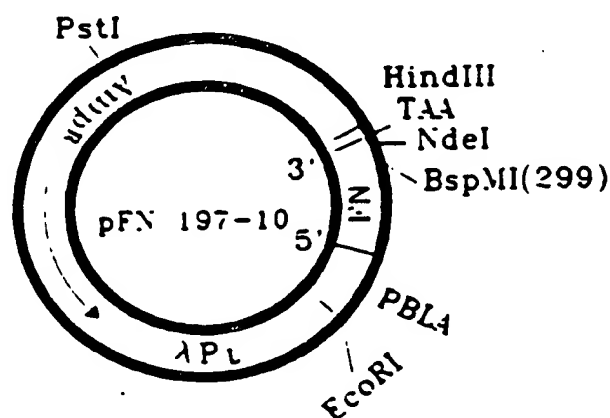
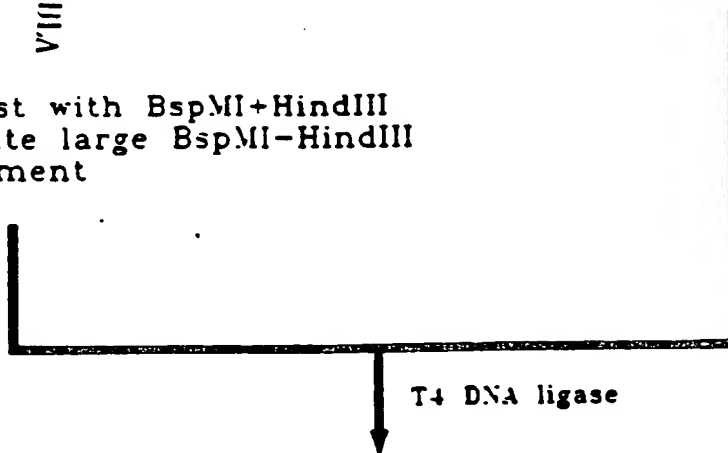


Figure 37

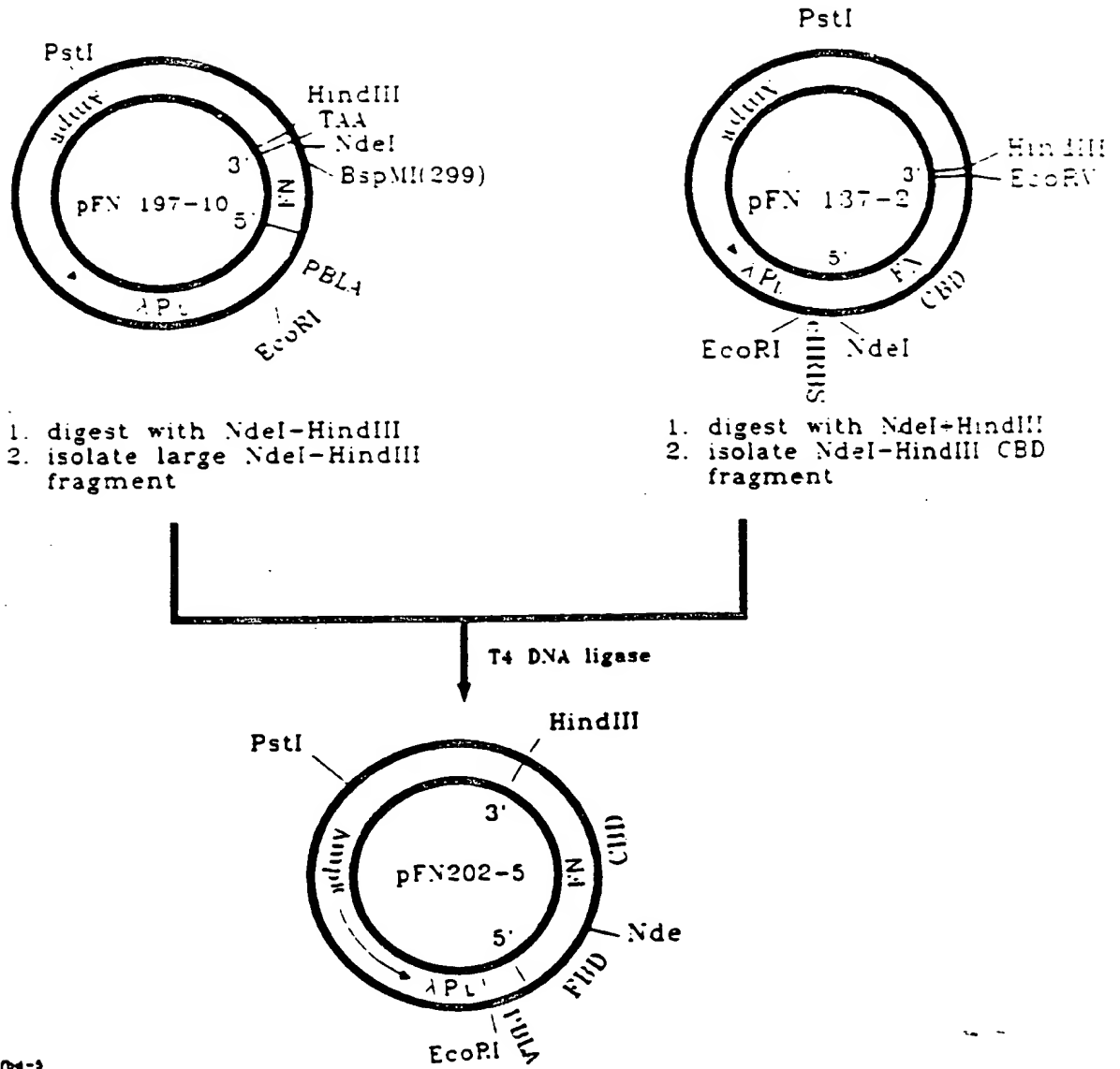


1. digest with BspMI+HindIII
2. isolate large BspMI-HindIII fragment



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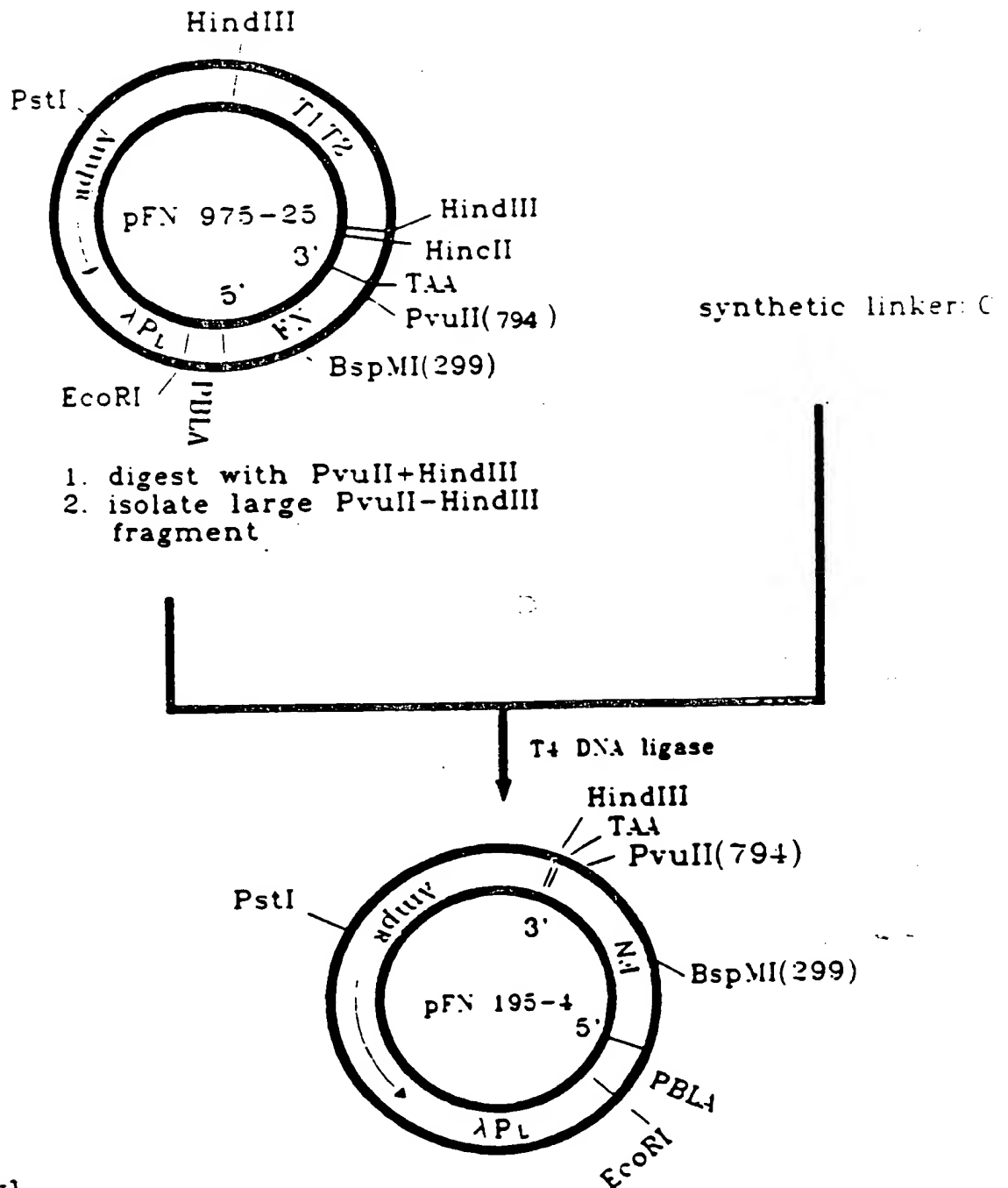
Figure 38



u/nd-5

002210-1626460

Figure 39



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Figure 40

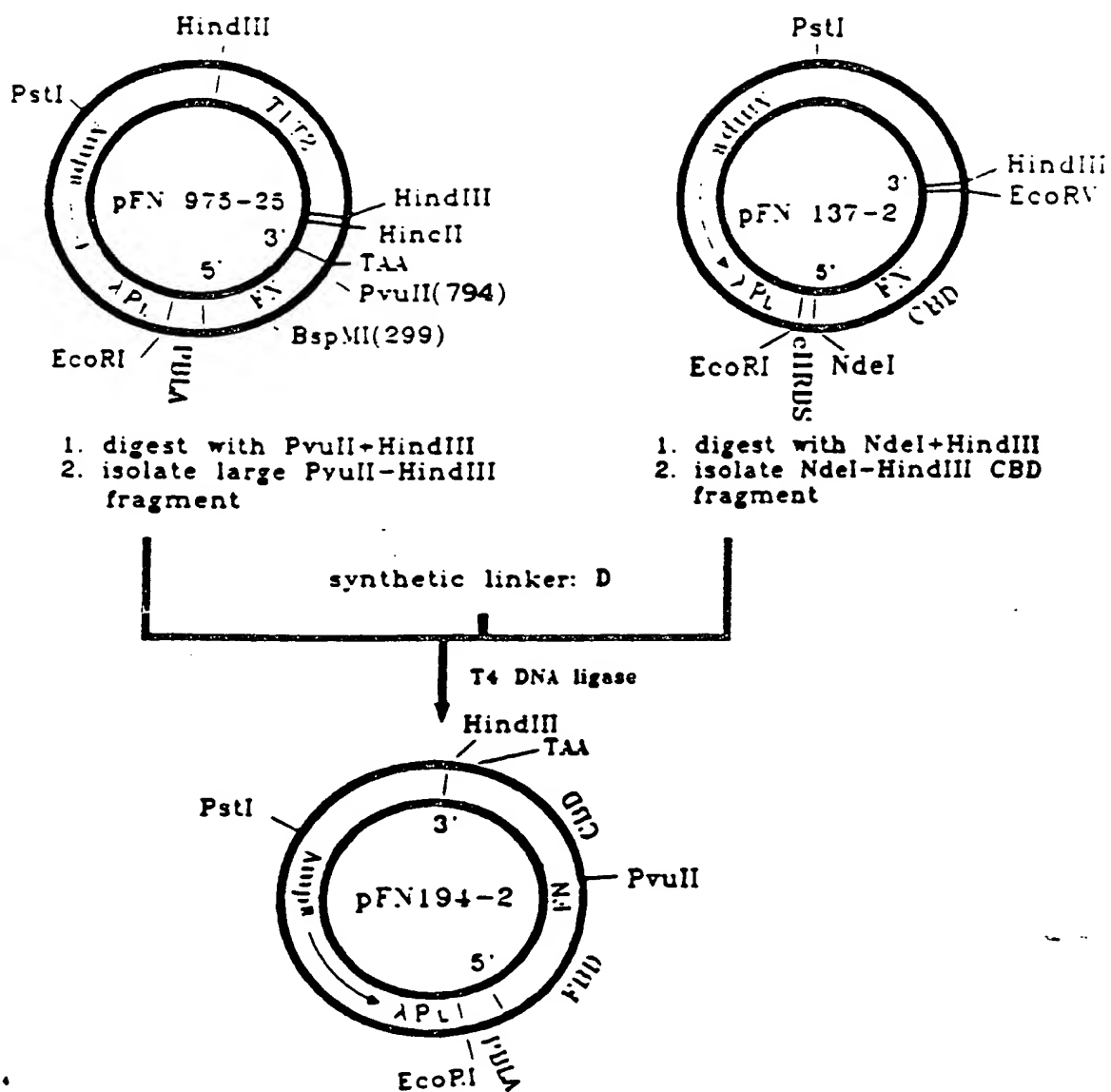


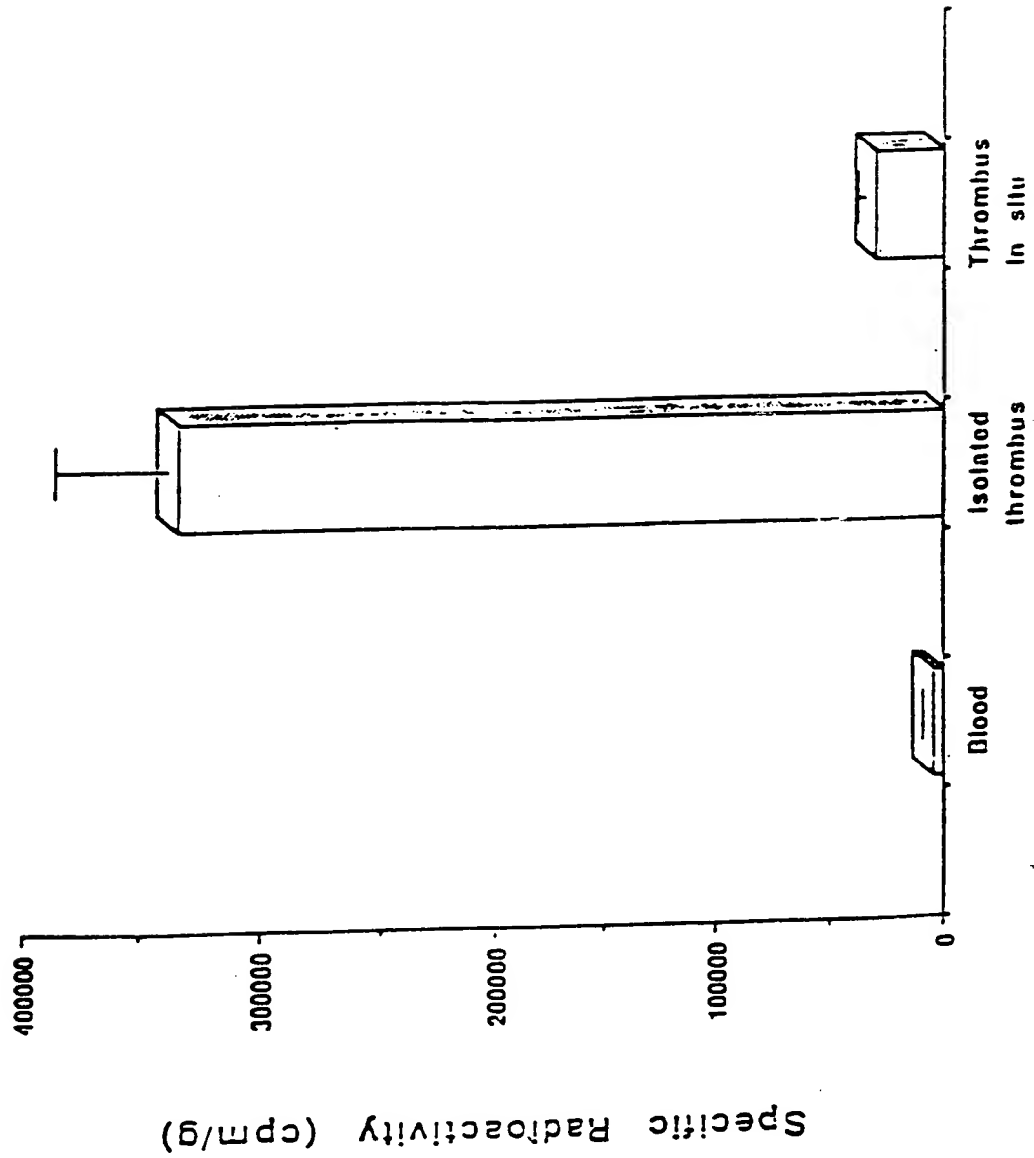
Figure 41

- A 5' GGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTAACAGCTGA 3'
3' ACCCGCTCCCTCTTATTTCGACATGGTAGCGTTTGGCGATTGTCGACTTCGA 5'
- B 5' GGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCCATATGTAAA 3'
3' ACCCGCTCCCTCTTATTTCGACATGGTAGCGTTTGGCGGTATACATTTTCGA 5'
- C 5' ATGGCCGTGGAGACAGCTAACAGCTGA 3'
3' TACCGGCACCTCTGTCTGATTGTCGACTTCGA 5'
- D 5' CTGTATACCAACC 3'
3' GACATATGGTTGGAT 5'

002210" T 2626460

Figur 42

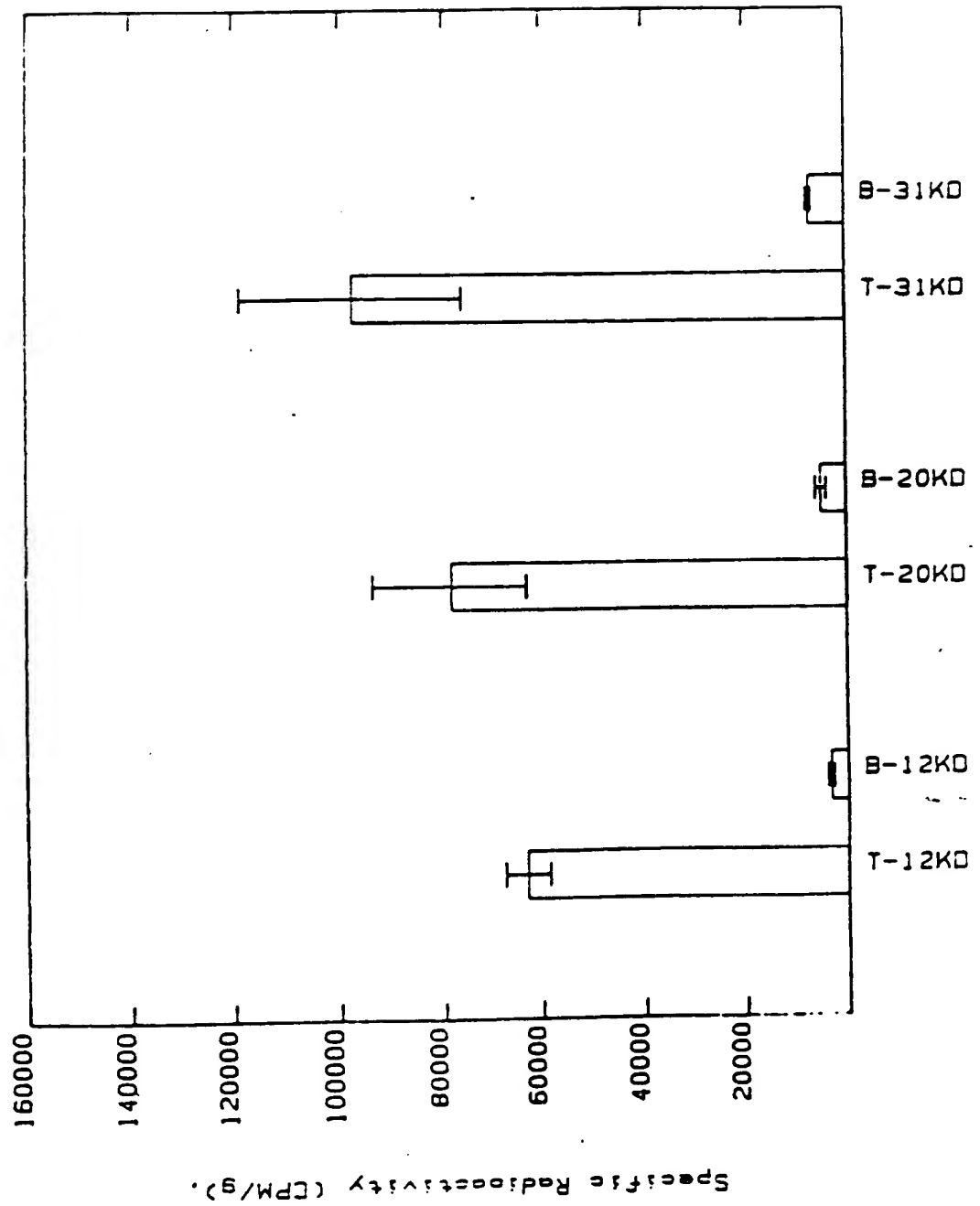
Uptake of Labeled 31KD rFBD by Blood Clots in the Rat Coil Model



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Figure 43

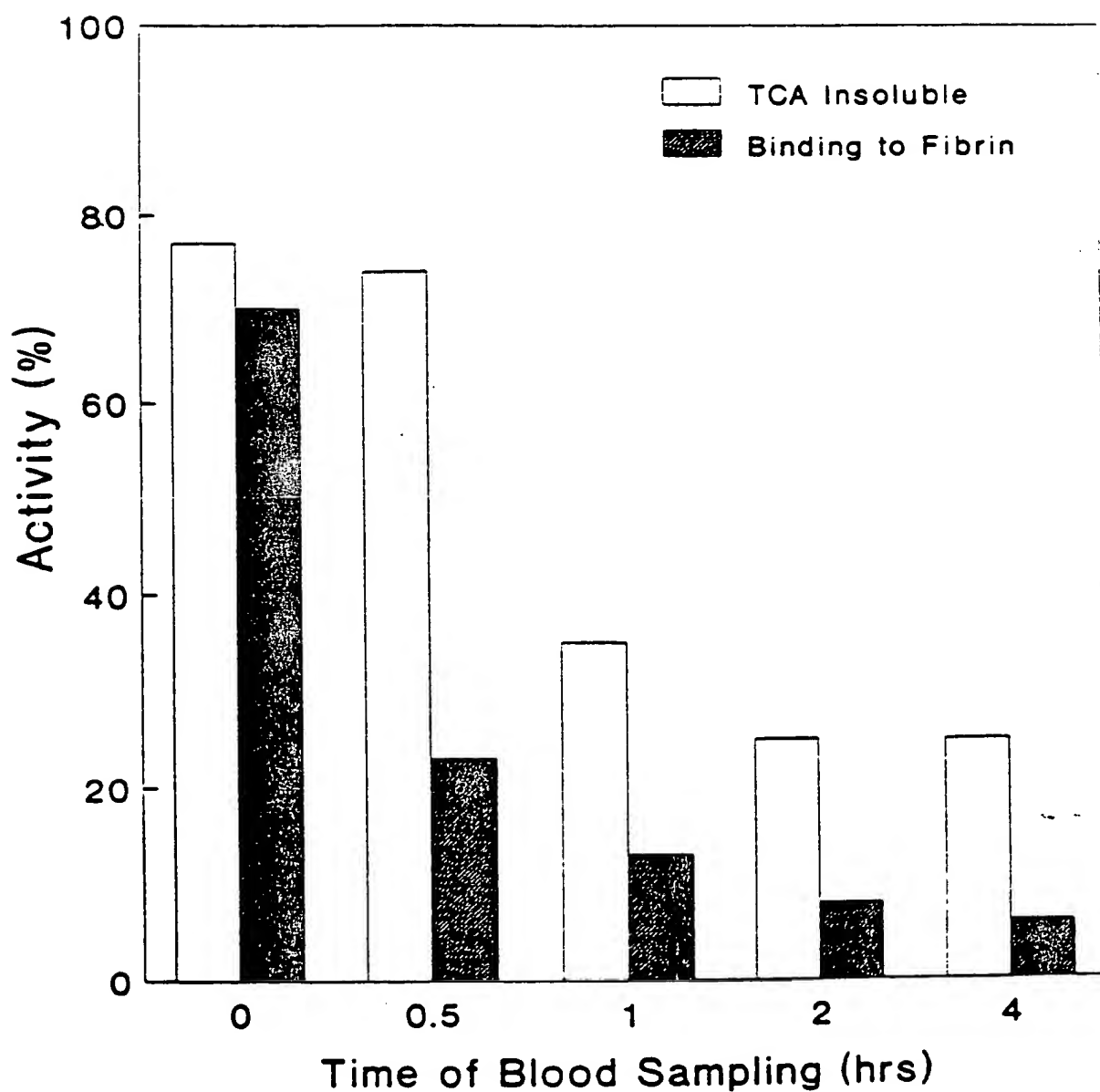
COMPARISON BETWEEN 12, 20 & 31KD FBD MOLECULES



09492971-012700

Figure 44

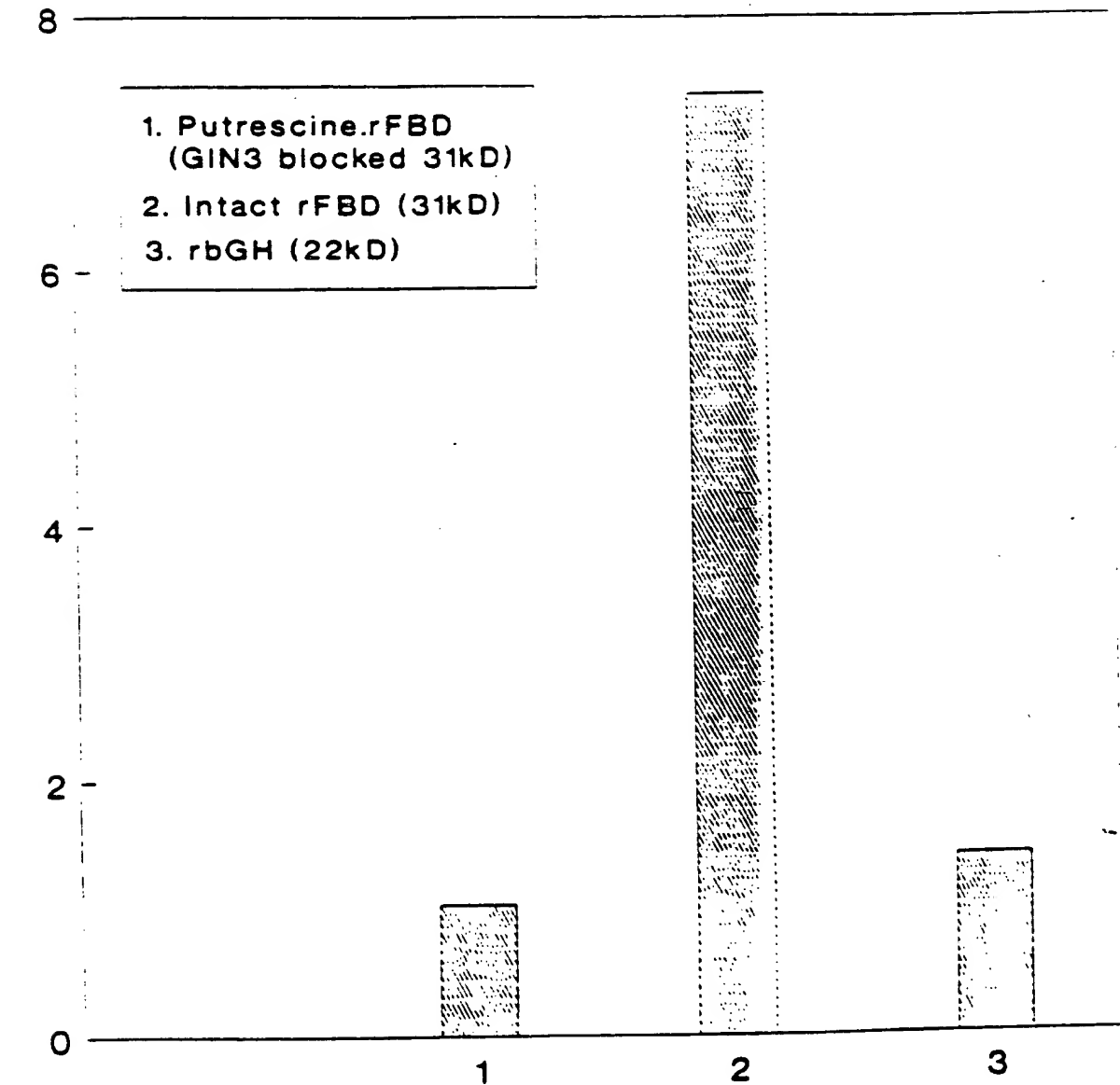
Metabolic Stability of rFBD in Rats;
Ex-vivo Binding to Fibrin vs. TCA
insolubility



ti-3/6/2

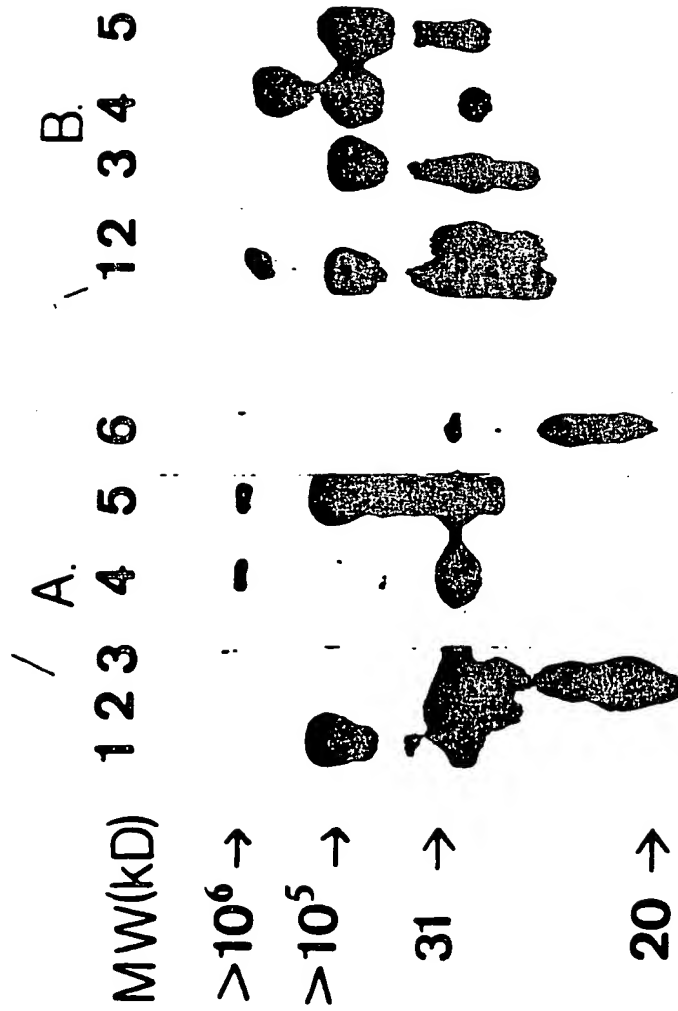
Figure 45

Specificity of binding to Fibrin;
Effect of T.G. on the binding of
rFBD vs. rbGH (Reaction II)



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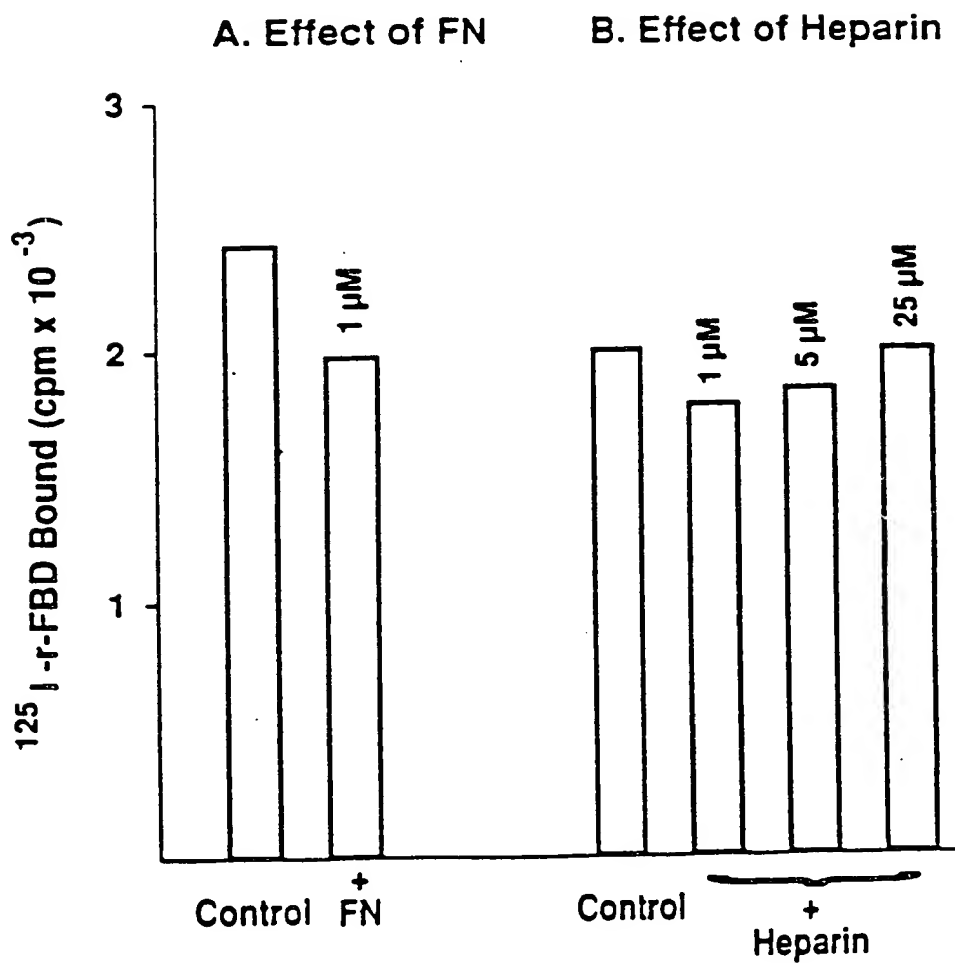
Figur 46



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Figure 47

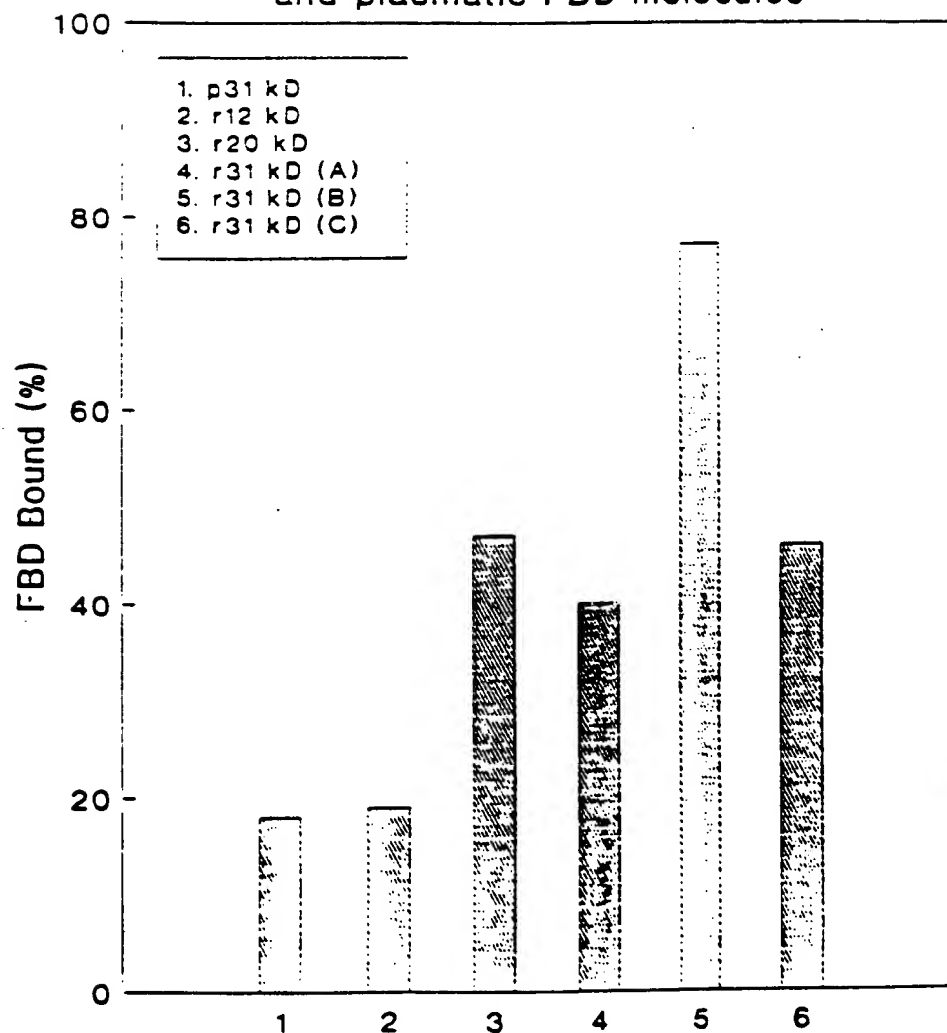
Binding of FBD to preformed clot (Reaction II);
Effect of FN and Heparin.



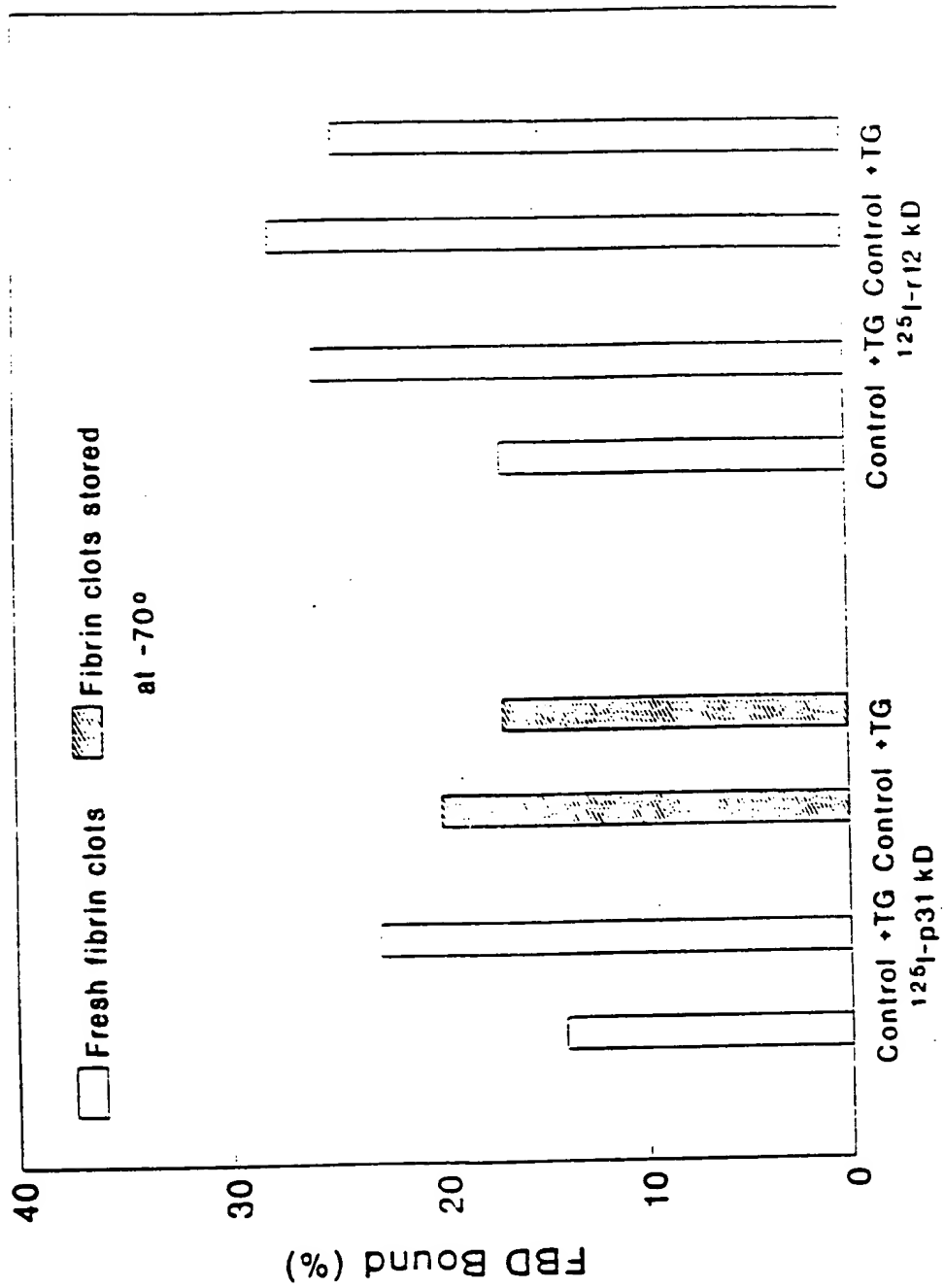
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Figure 48

Binding of FBD to Fibrin clot (reaction II);
comparison between various recombinant
and plasmatic FBD molecules



Binding of FBD to Fibrin clot (reaction II);
Comparison between fresh and frozen Fibrin clots

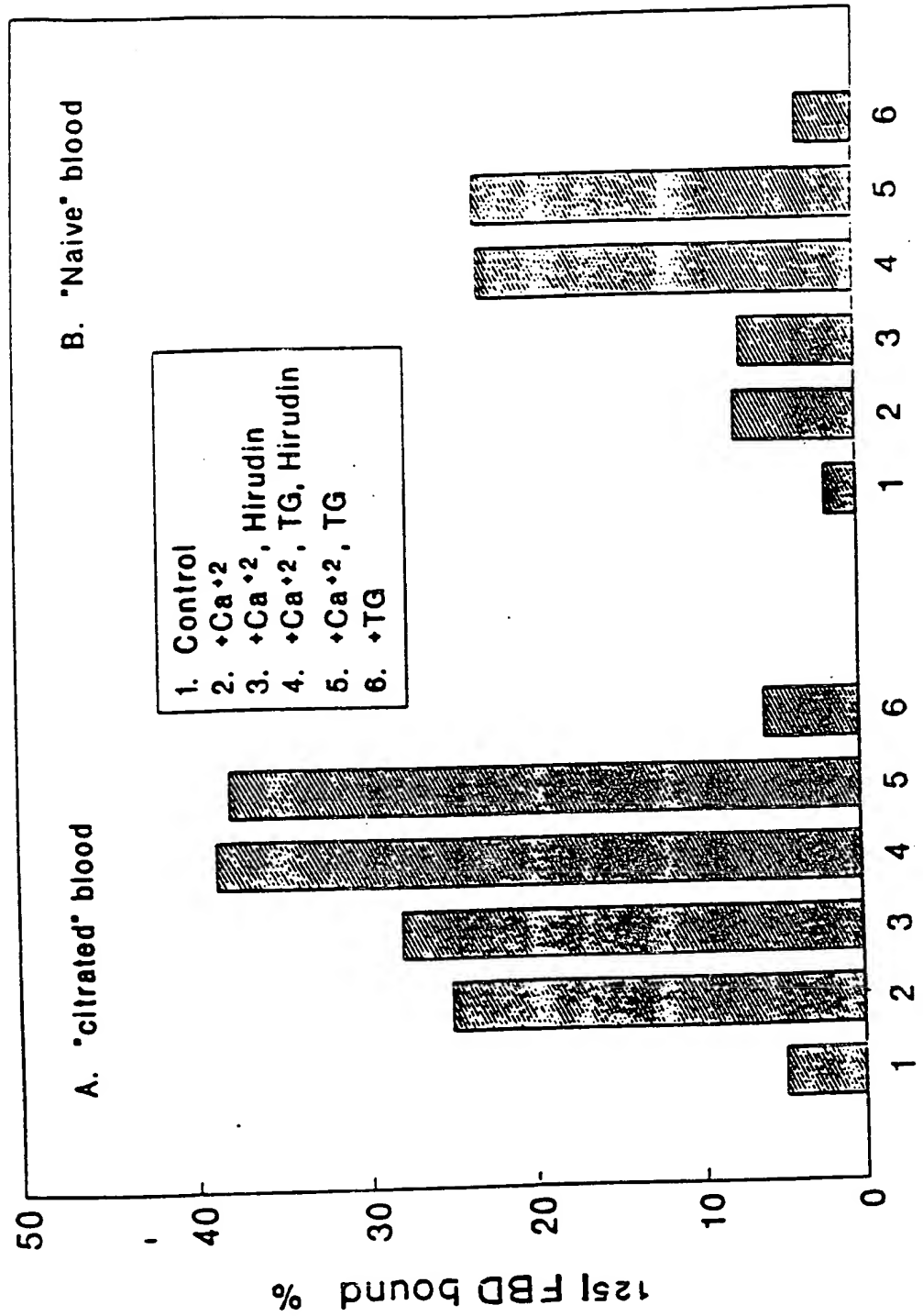


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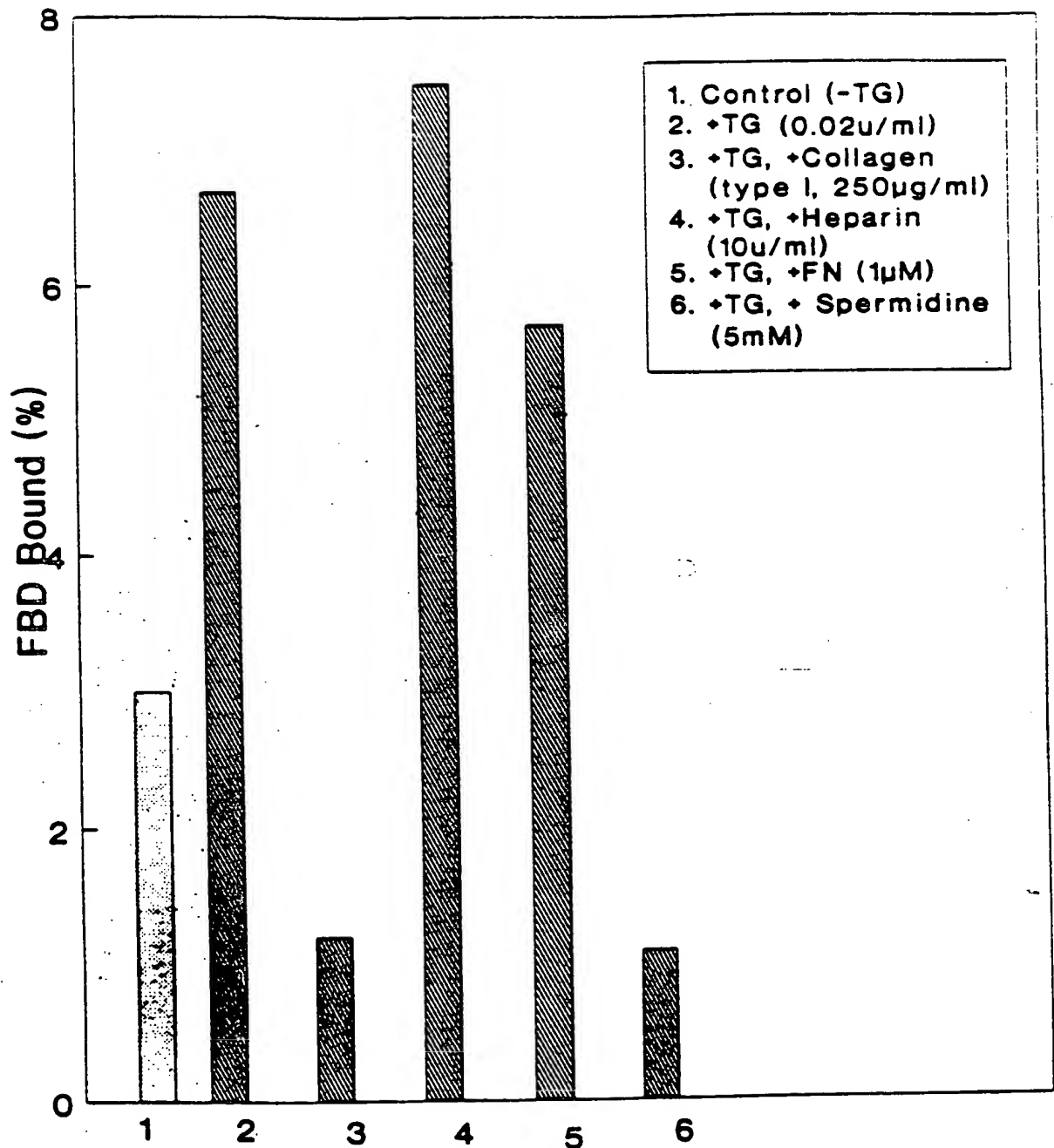
Figure 50

Binding of FBD to Fibrin (Reaction II)



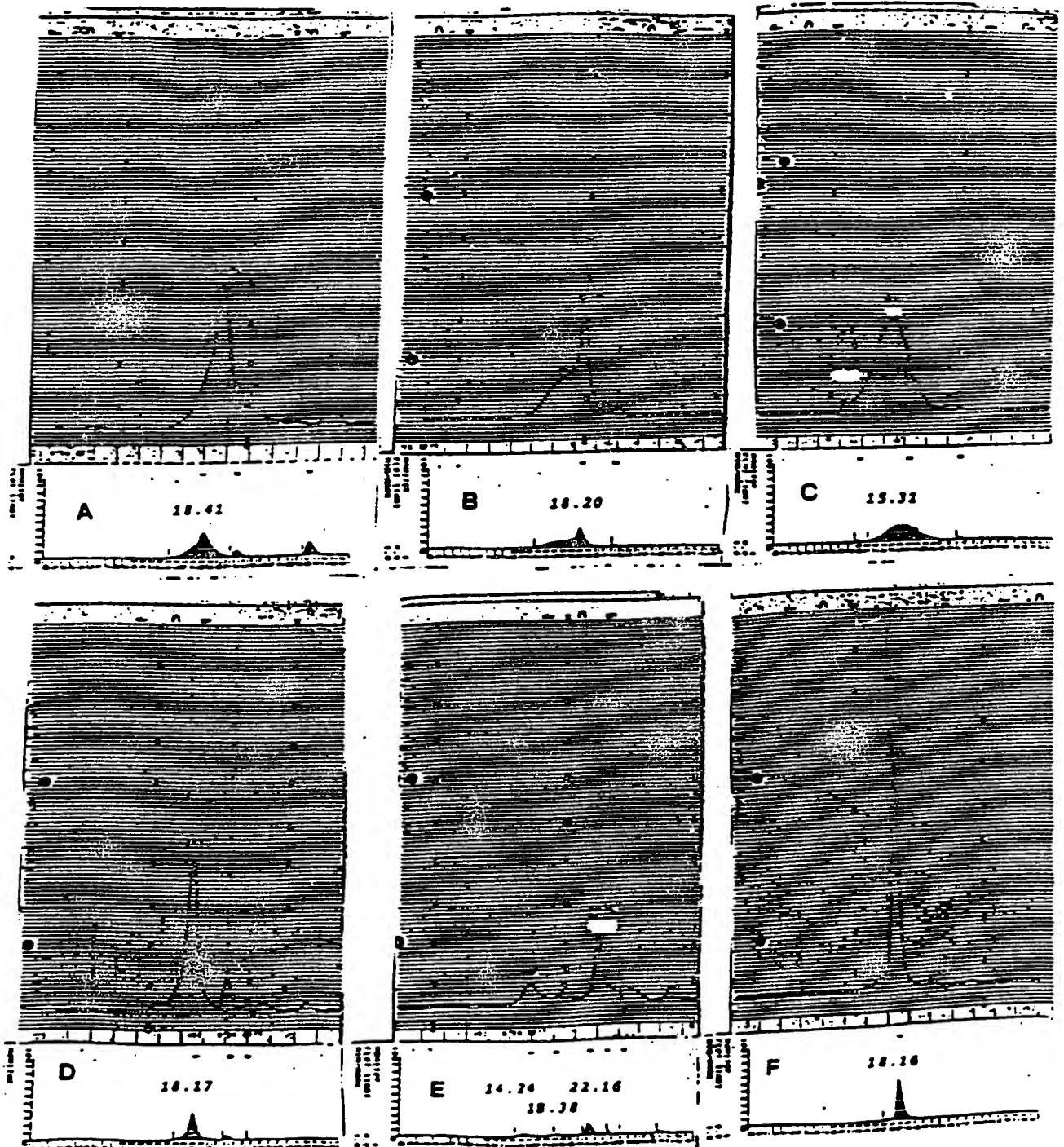
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r-FBD binding to ECM



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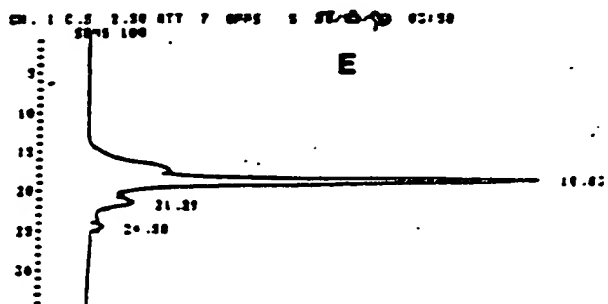
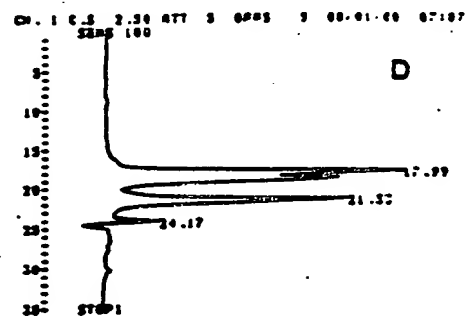
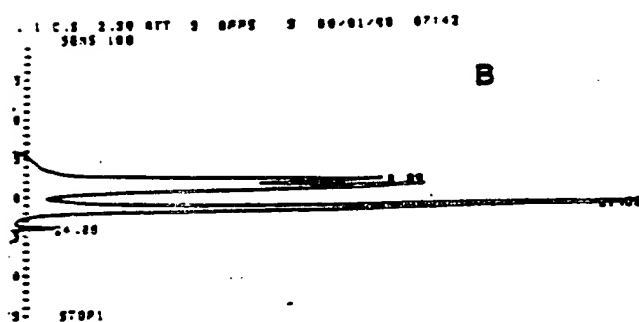
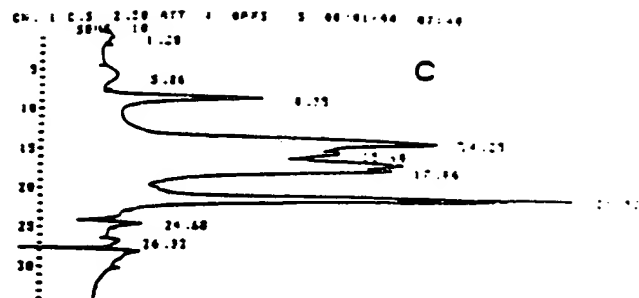
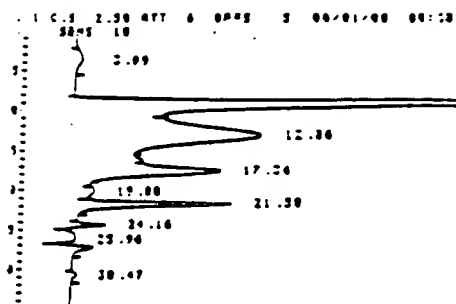
Figure 52



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Figure 53



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